Recommended Nutrient Intakes for Canadians

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I. INTRODUCTION

In Canada, it has been customary to refer to the publication of recommended nutrient intakes as the dietary standard. This terminology has led to confusion with various *dietary guides* describing patterns of food use rather than nutrient requirements. The present revision adopts a new title, Recommended Nutrient Intakes for Canadians. Although this title is incomplete in that it does not give recognition to a discussion of energy, the committee members hope that it will help to avoid some of the past confusion.

The Dietary Standard for Canada was revised in 1975 by a committee established in 1972. At that time a recommendation was offered and accepted that in approximately 5 years the standard should be reviewed and, if deemed appropriate, further revised in the light of additional knowledge. Accordingly, an *ad hoc* advisory committee was established to review the standard in 1979. This committee sought advice from the professional community across Canada concerning difficulties encountered in the use of the standard, new information, whether published or not, and recommendations for material to be included in such documents in the future. Late in 1979 the committee recommended that a full review and revision of the Dietary Standard for Canada be undertaken, and the recommendation was accepted.

The advisory committee followed the practice of the previous committee by inviting knowledgeable individuals to draft specific chapters and to send them to colleagues for review and comment. The revised chapters were then used by the committee as the basis for the final report. Although contributions to individual chapters are not shown, authors and reviewers are named in Acknowledgments.

The committee emphasizes that users of this document should examine the text with great care. For many nutrients there are important qualifications about the interpretation of the recommendations and suggestions about how these should be adjusted to fit particular situations. Users are urged also to consider with great care the definitions offered below and the section on the applicability and appropriate use of the recommended intakes. It is the hope of the committee that if these sections are clearly understood many of the problems that have surrounded the use and misuse of the standard in the past will be avoided.

Definitions of Terminology and Concepts

There has been considerable confusion and no clear agreement about terms used in the Dietary Standard for Canada and in the nutrition literature in general. The committee offers the following explanation of terms used in the present report in an attempt to add clarity to its interpretation.

Requirement Requirement is taken to mean that level of dietary intake of a nutrient that meets an individual's need, described as the establishment and maintenance of a reasonable level in tissues or stores in the body. In the case of energy, the requirement is considered to be the level of intake needed to maintain appropriate body size and composition and to meet the energy required for expected work and leisure activity.

For infants, children and pregnant women, requirement is meant to include needs for the deposition of new tissues, and in lactating women, for the production of milk.

As here described, requirements refer to levels of intake needed to *maintain health in already healthy individuals*. For this purpose, health is considered to be more than the absence of clinically apparent ill health. In the estimation of requirements, health is taken to include the establishment and maintenance of reasonable levels of the nutrients in body tissues (stores). Requirements so estimated are higher than amounts needed to prevent clinical deficiency disease. Failure of an individual to meet his or her requirement for health as thus defined may result in depletion of body stores without the development of clinically apparent disease. More severe deprivation might be expected to result in clinical signs. The estimates of requirements are inappropriate for persons recovering from previous depletion or undernutrition and they may be inappropriate for those with diseases that interfere with the absorption, utilization or excretion of nutrients. Except when discussed in the text, they do not take into account possible interactions between drugs and nutrients.

Among normal individuals, the requirements for many nutrients are affected by the nature of the diet, body size, activity, age, sex and physiological state. It is customary to describe the general characteristics of the type of individual for whom an estimated requirement is provided. Some of the assumptions made in describing such individuals and situations are outlined in a later section.

Individual Variability of Requirement Requirements for energy and for nutrients vary among individuals of comparable body size, physical activity, dietary pattern and of the same age and sex. This is termed individual variability of requirement. Thus the requirements of a group of similar individuals will show a range and the average for the group may be stated.

Average Requirement The average requirement represents the mean for a group of individuals with specified characteristics. It should be recognized that particular individuals within such groups will have a requirement differing from the average for the group.

In the case of energy, it is customary to state the average requirement. It follows that in a group of generally similar individuals approximately half would be expected to have actual requirements above the average and half below it. This approach is taken because there is a risk to health from inadequate or excess intakes of sources of energy.

Recommended Nutrient Intake A recommended nutrient intake (RNI) is taken as the level of dietary intake thought to be sufficiently high to meet the requirements of almost all individuals in a group with specified characteristics (age, sex, body size, physical activity, type of diet). It takes into account individual variability. Of necessity the RNI exceeds the requirement of almost all individuals. It follows that an intake below the recommended amount does not mean that the individual has failed to meet his or her requirement, but the lower the intake in relation to the RNI, the greater the risk that the individual has not met his or her requirement.

In the case of nutrients, it is customary to state the recommended nutrient intake. Of necessity, the RNI exceeds the actual requirement of almost all individuals in a group having similar characteristics. This approach is taken because risk to health is associated primarily with inadequate intakes.

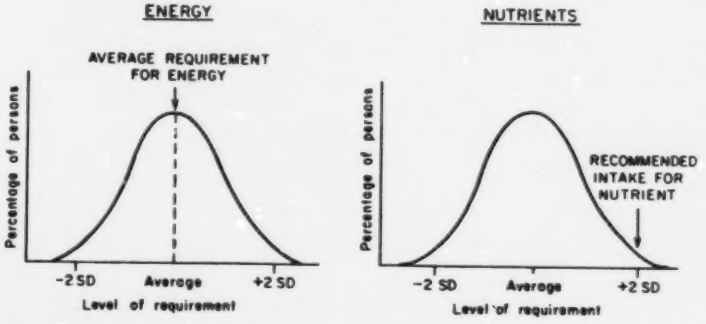

Figure I.1. Comparison of average requirement for energy and recommended intake of a nutrient. It is assumed that in each case individual requirements are normally distributed about the mean.

These concepts are illustrated in Figure I.1. An additional reason for the difference in approach to the description of requirements for nutrients and for energy is that in the latter instance there is reason to believe that physiological mechanisms operate to maintain the intake near the level of requirement. Furthermore, an imbalance between an individual's energy intake and requirement can be assessed in terms of change in body size or composition. Neither of these circumstances appears to be applicable to nutrients.

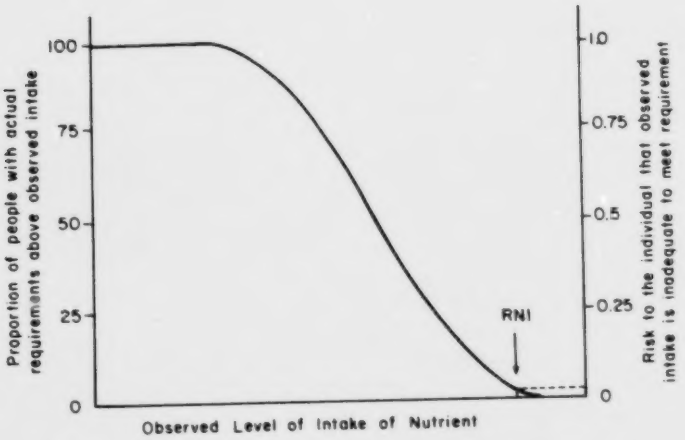

Figure I.2. The concept of risk applied to a recommended nutrient intake (RNI). If it is assumed that individual requirements are normally distributed about the mean and that the RNI is set at the average requirement + 2 standard deviations, the probability of inadequate intake (risk) of an individual ingesting the RNI would be 0.025, *i. e.*, 2.5% of persons would be expected to have a requirement above this level.

Risk of Inadequacy From the above discussion it follows that risk is taken to mean the chance that a given level of intake is inadequate to meet the actual requirement of an individual. This is a probability statement. It is not a measure of severity of any inadequacy that may exist. The concept of risk of inadequate intake is portrayed in Figure I.2. The RNI is a statement of a requirement associated with a low risk of inadequacy to any individual in a specified class of people.

Excessive Intake For some nutrients there are known detrimental or toxic effects of high intakes. In most cases these are much higher than the RNI but in a few they may be close to it. As with the concept of

nutrient requirement, it is to be expected that there is individual variability associated with the definition of excess intake, hence a risk that may be portrayed by a curve analogous to that in Figure I.2 except that it moves in the opposite direction. Conceptually, the body can adapt to all intakes between the RNI and the level of excessive intake without apparent harm, but below and above these the risk of detrimental effect for any individual increases (*i.e.*, an increasing proportion of individuals in a specified group would be adversely affected).

Safe Range of Intake Conceptually, then, there is a range of intake for each nutrient that is associated with low risk, to the individual, of either inadequate or excessive intake. An individual's intake should fall within that range.

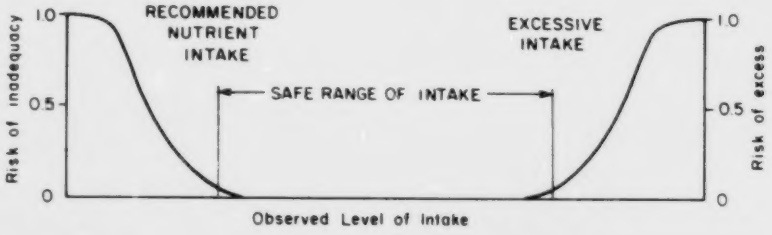

Figure I.3. The concept of a safe range of intakes. It is assumed that there is individual variability of both requirement for a nutrient and tolerance for high intake, hence that risk curves for inadequacy and excess may be described as in Figure I.2. The safe range of intakes is associated with a very low probability of either inadequacy or excess for an individual.

For most nutrients it is not possible at present to describe with confidence the upper limit of this range of safe intakes. The present statement is limited to presentation of estimates of the lower limit, the RNI, with the inference that intakes at or somewhat above these levels will be safe and appropriate. (Note that the concept differs in the case of energy, for which it is assumed that for an individual, risk is associated with a small departure from actual requirement in either direction.) The concept of a safe range of intake is illustrated in Figure I.3. The term optimal intake is not used in this report because in the opinion of the committee there probably is no such thing. Rather, as indicated above, it is the opinion of the committee that there is a safe range of intakes within which there is no particular one that confers an advantage upon any individual.

It is to be hoped that as knowledge increases it will be possible to give a better description of a safe range of intakes and that the concept of optimal intake will be forgotten.

Conditions, Qualifications and Special Considerations

Time Frame for Recommended Intakes

It is customary to describe requirements for energy and nutrients as a rate of intake per day. There is, however, no indication that these levels of intake should be ingested *each* day. Rather, requirements are measured and RNI's are expressed in terms of *usual* intakes, the average intake over many days or weeks. In a practical situation it would be expected that an individual's intake would vary from day to day. It follows that in applying estimates of requirements in the planning or assessment of diets of individuals, the average level of intake over a number of days should be considered. This has been discussed by Beaton *et al.* (1).

Nature of the Diet Consumed

As discussed in the text, the nature of the diet is one of the factors that influence the requirements for some nutrients. For example, the bioavailability of iron and zinc and the biological value of the dietary protein are directly affected by the mixture of foods consumed.

For the purpose of presenting summary tables it is necessary to make an assumption about what may be called a typical dietary pattern. The present report has drawn upon information about food disappearance *per capita* in Canada (2) and the pattern of food intake recorded in Nutrition Canada (3).

The user of this report is cautioned to recognize that tabulated estimates of requirements may not apply to dietary situations that are markedly atypical. The text should be consulted for guidance in such cases.

It is not possible at present to describe in quantitative terms all of the nutrient-nutrient and nutrient-non-nutrient interactions associated with food. The inherent assumption here is that the nutrients discussed are components of a diverse diet. Although the estimated requirements are useful guidelines in the consideration of pharmaceutical preparations or formulated foods, it is possible that an unusually high intakes of some nutrient may affect the requirements for others.

Unrecognized Nutrients

Although knowledge of quantitative requirements is incomplete,

it appears likely that all of the nutrients of practical importance in the human diet have been identified. For example, it is now possible to sustain clinical patients with chemically defined intravenous solutions, with no food intake by mouth, for a period of years.

Assumed Body Size and Growth Rate

Requirements for many nutrients are affected by body size (and body composition) in the adult and by both existing body size and growth rate in the child. In the text, for a number of nutrients, guidance is offered with regard to adjustment of requirements for differing body size. In suggestions of allowances for growth, the apparent coefficient of variation of growth rate, about 15%, has been taken into account. In an analogous manner, the variability of intrauterine growth rate has been taken into account by acceptance of the coefficient of variation of birth weight, about 15%. These allowances may be somewhat inappropriate for the few exceptional individuals who differ from the average growth rate by more than 30%. Such a situation may hold with regard to the relatively brief period of the growth spurt at adolescence. In the tabulations, the individual peak rates of growth may be masked by the averages for groups classified in age intervals.

Anthropometric descriptors are presented as typical values for particular age and sex groups without implication that they are optimal or desirable. The age groupings adopted are arbitrary in nature. The choice of intervals is based upon such considerations as increments in body size in proportion to attained body size in children, physiological changes such as puberty and menopause, and social factors. (See section on energy (II).)

It is the assumption of the committee that, except for specified physiological changes such as puberty and pregnancy, requirements change with age. The estimated requirements refer to the *mid-points* of the age intervals shown. A danger from an increased number of tabulated values may be an impression of greater precision of the estimates than is justified by the data available. The committee urges that the user of these figures guard against such an interpretation.

Volume of Breast Milk

To estimate the nutrient requirements of lactating women and to confirm the suitability of estimated requirements for young infants, it is necessary to have information about the volume and composition of the breast milk secreted. Past reports have assumed an average volume of 850 mL/day at full lactation. In the present report, based upon data from well-nourished women in Sweden (4,5,) and the United States (6), it is taken that at full lactation (3 or more months), the average milk secretion (milk intake of an infant fed exclusively from the breast) is

about 750 mL/day with a coefficient of variation of about 15%. At 1 month, the average volume is a little more than 600 mL/day.

Judgmental Nature of Estimated Requirements

This document is the report of an advisory committee. In preparing the report, members of the committee drew upon the advice and experience of many colleagues as well as published information on human nutrient requirements. It must be emphasized, however, that at present the information is fragmentary. In the preparation of the report it has been necessary to make judgments about probable levels of requirement, probable levels of absorption, probable differences imposed by age and sex, etc. It is to be accepted, then, that the final estimated requirements given here are judgmental in nature. As further direct and indirect information becomes available, judgments by future committees may differ from those offered here as some of the present judgments differ from those of the past.

In the text of the report an attempt has been made to show the basis of current judgments. The amount of detail in some of these discussions should not be taken to imply great precision of knowledge about requirements. It may reflect a sufficient volume of information to document the gaps in present knowledge about which judgmental decisions must be taken.

Throughout the report, the committee has attempted to test its judgments by asking the question "Is the estimated requirement apparently consistent with experience in the free-living population?" Although information permits only an imperfect answer, it has tempered judgments and recommendations.

Interpretation and Use of the Recommended Intakes

This document, Recommended Nutrient Intakes for Canadians, has been designed to fulfil several functions. Proper use of it requires a full understanding of its meaning.

The Dietary Standard for Canada has been widely used in planning diets and processing food supplies for individuals and groups. At the level of the individual, the RNI is the appropriate target for the lower level of planned intake (usual intake over a reasonable period of time) because it offers an assurance of a low level of risk of inadequate intake. The same approach cannot be used for energy, for which figures are estimates of *average* requirements and consequently an individual may need and consume more or less. Unlike the recommendation for a nutrient for which there is a range of appropriate intakes with a suggested level that meets the needs of most people, an average value for energy intake is not suitable for an individual, but the history

of intake in relation to body weight and activity is an appropriate basis. At the group level, the average energy intake should provide a reasonable estimate of the average requirement that can be expected. The actual intakes of nutrients will be affected by the consumption of energy, and on a group basis will also show a probability distribution. Different considerations are therefore involved in advising an individual or a group and in dealing with a recommended nutrient intake or an average energy requirement.

The dietary standard has been used also, in conjunction with information about the distribution of age and sex within the population, to provide estimates of the total needs of the population for energy and nutrients (*per capita* requirements). Care must be taken in the use of such estimates since they do not take into account the distribution of either requirements or intakes among individuals. There is no assurance that a food supply for a population that appears to meet the *per capita* requirements for nutrients will meet the needs of all individuals in the population after distribution of intakes is taken into account. Nevertheless, with these constraints in mind, such a standard may be used to provide a first consideration of the possible effect upon nutrition of changes in food supplies that might result from various policy decisions.

With information about the actual or probable distribution of food consumption and nutrient intakes, the recommended intakes may be used in judging the need for and the amounts used in programs of food fortification and supplementation and other interventions in public health. The recommendations may be of use in establishing desirable standards for foods or in considering appropriate statements to be made in advertising.

Such standards and recommendations are and can be used in assessing the probable adequacy of observed intakes of food, but in this great caution must be taken. There has been a tendency to misinterpret such recommendations when thus applied. In the case of nutrients, since the RNI's have been set sufficiently high to cover the requirements of almost all individuals, they exceed the actual requirements of almost all. It follows, therefore, that if an individual's intake of a nutrient is below the RNI, this does not necessarily mean that that individual *is* inadequately nourished. It means only that he or she *may be* inadequately nourished. The further the observed intake falls below the RNI, the greater is the probability that that person is undernourished (see Figure I.2). If the distribution of requirements in a population group is known or can be assumed with reasonable reliability then actual probability statements may be attached to the judgment of adequacy, and, for a group, an estimate can be made of the proportion that is likely to have inadequate intakes (even though it is

not possible to identify which individuals have inadequate intakes). Such judgments form the basis of individual dietary counselling and of the assessment of existing dietary practices.

In the case of energy, it must always be remembered that the figures represent average requirements. Even after adjustment for body size, level of activity and other variables, it must be recognized that there is equal chance that the individual's requirement will be above or below the estimated requirement. This is important in both counselling and assessment.

It is not possible to judge nutritional status on the basis of dietary intake. Poor nutritional status is a state of health consequent to inappropriate dietary practice or ineffective utilization of a nutrient and must be judged through biochemical, anthropometric and clinical approaches.

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II. ENERGY

The body needs energy for the synthesis of structural and other materials such as secretions and excretions; for activity at the level of cells, tissues, organs and of the whole organism; for external work, and for the maintenance of body temperature. These needs are interrelated and cannot be measured separately.

The requirement for energy is proportional to the body size and is commonly expressed in relation to weight, surface area or lean body mass. Several other factors govern the need for energy, among the most important being age, physiological state and physical activity. Cell turnover and rates of synthesis in the body are highest during growth and decrease with advancing age, and per unit of size, the requirement for energy decreases from infancy to old age. Pregnancy and lactation increase the quantities of materials synthesized in the body and consequently the need for energy. The need for energy increases with the level of activity and the magnitude of this increase varies with age, training and climatic conditions. Adaptation to a cold or a hot environment through physiological mechanisms such as shivering and sweating increases the requirement for energy, but this increase is often negligible because people usually can protect themselves against extreme variations in temperature.

Body size, age and, to some extent, the degree of physical activity are measureable and their effects on the need for energy can be estimated. Other factors that are known to contribute appreciably to the energy requirement cannot be evaluated with any degree of precision. These include the level of metabolism that is set by genetic and environmental factors, including the plane of nutrition; the composition of the diet, and various degrees of stress. These affect the need for energy by modifying the activity of certain organs and the rates of synthesis of certain secretions or by including more or less efficient metabolic pathways.

Over a long period of time, if the size and composition of the body remain constant, the intake and expenditure of energy equilibrate, so that information on either side of the equation under those conditions provides a good estimate of the requirement. Because of large interindividual differences in energy intakes, however (the coefficient of variation among North American adults is about 25% (1)), simple

extrapolation of such figures to other groups or to a general population may not be valid. Even within the same age-sex group, energy requirements per day expressed in relation to body weight have been found to show a coefficient of variation of about 15% (2). Energy requirements, therefore, are best expressed as a range for a given group defined by age, sex, body size and level of activity. Within this range the requirement of any individual cannot be determined precisely, and an amount of energy based upon a rough estimate from physical characteristics cannot be depended upon to maintain weight over a long period (3).

Energy for the body is derived from organic compounds present in foods. According to the Nutrition Canada survey (4), protein provides 14% of the energy consumed by Canadian adults, fats 40% and carbohydrates and alcohol 46%. According to statistics of sales of alcoholic beverages, the average Canadian of age 15 years or over consumes 2.6 gallons (about 11.7 L) of ethanol per year (5), equivalent to 225 kcal/day (945 kJ/day).

The Unit of Energy in Nutrition

It was recommended (6) that the kilojoule (kJ) be the unit of food energy to replace the kilocalorie (kcal) because *le Système international d'unités* (SI) had been adopted as the standard of weights and measures and in that system the joule (J) is the unit for all forms of energy. The fact that the calorie (cal) is and always has been defined in terms of the joule strengthens support for the change. Since the present situation is one of transition, however, both the calorie and the joule, in the forms of their appropriate multiple units, are used in these recommendations.

The joule is a newton metre (N m), and in terms of base units of the SI it is 1 kg m^2 s^{-2}. One calorie equals 4.184 J, and 1000 cal = 1 kcal = 4184 J = 4.184 kJ = 0.004 184 megajoule (MJ). Accordingly, the Atwater energy conversion factors of 4 kcal/g of protein or carbohydrate and 9 kcal/g of fat for mixed diets become 17 and 37 kJ/g respectively.

Average Requirements for Energy

Adults

As indicated in the introduction to this chapter, average energy requirements of people grouped according to age, sex, body size and activity can be validly estimated from data on the energy intake or expenditure of large numbers of individuals with similar characteristics. The figures presented in Table II.1 are based on the observed intakes of energy by large groups of Canadians presumed to be healthy and in energy equilibrium (7-9).

Unlike the recommended intakes of nutrients, which are set at a level approximately 2 standard deviations (SD) above the average

requirement, these figures are *averages*. The reason for using averages in the case of energy is that there are risks of malnutrition from intakes on either side of the mean, the probability of overnutrition being even higher than that of undernutrition. Actual requirements of Canadians are presumed to lie within a range of ± 30% (2 SD) of the averages given per unit of body weight.

There is no information on the activity pattern of the subjects of the studies forming the basis for the figures presented in Table II.1, nor are there any data on the average activity of Canadians. From a general knowledge of the latter, however, a model (Table II.2) can be elaborated to describe the pattern of activity corresponding to the energy requirements defined in Table II.1. The average energy requirements presented in Table II.1 are those amounts deemed necessary to maintain the current average activities of Canadians, but without proper criteria for determining desirable levels of activity, no recommendation can be made on the advisability of maintaining or changing this pattern.

The heights and weights of adults shown in Table II.1 are derived from smooth curves based on the Nutrition Canada survey (10). The decrease in the energy requirement with age reflects a decrease in the rate of resting metabolism, which is equivalent to 2-3% per decade from early childhood to old age (11), and also a decrease in activity that may vary greatly from one individual to another.

The average intakes of energy suggested in Table II.1 can serve as a basis for planning diets or determining food supplies for groups of people of the same age, sex and body weight as those described in the same table and carrying out an activity comparable to that outlined in Table II.2. The fact that a diet or a given food supply yields the amount of energy indicated in Table II.1 does not guarantee, however, that everyone in the group consuming that diet will meet his or her energy requirement, because there is no way to know where an individual's need stands on the distribution curve of energy requirements of the group to which he or she belongs. Inter-individual variation is large and only a portion of it can be explained by measurable factors such as age and body size. Small differences in physical activity are not easily detected and the effects of adaptation to various levels of energy intake are difficult to evaluate.

Thus, it is clear that Table II.1 cannot be used to estimate an individual's energy requirement for the purpose of assessing his or her energy status and offering dietary advice. Anthropometric measurement is the only valid index of energy status. The actual body weight compared with the desirable weight for age, sex and height indicates whether over a long period the intake of energy has been higher, lower than or equal to the requirement. Tables of such desirable weights for adult men and women are available for making this comparison (12). If

the body weight remains stable, it can be assumed that the intake and expenditure of energy are in balance, regardless of the ponderal status. The only way to evaluate a person's energy requirement is therefore to determine by observation over a certain length of time the level of intake necessary for maintaining the body weight when activity is at the desired level.

When the figures of Table II.1 are used with the limitations set out above, adjustments for body size can be made by calculating the daily requirements using the figure expressed as per kilogram of body weight. If an adjustment for activity appears necessary, one can estimate the daily requirements using the rates of energy expenditure given in Table II.2 but modifying the number of hours spent at each type of activity according to the pattern characteristic of the group that is being considered.

Pregnancy

The energy cost of a human pregnancy during which there is a gain in weight of 12.5 kg has been estimated to be 80 000 kcal (335 MJ), approximately half of which is due to an accumulation of fat in the mother (13). In countries where food is abundant and where few women breastfeed their infants there is a tendency to consider this storage of potential energy as non-essential and perhaps undesirable. Furthermore, in these parts of the world it is commonly thought that women reduce their activity during at least the last 2 or 3 months of pregnancy. For these reasons, the total energy cost of pregnancy has been estimated as 40 000 kcal (167 MJ) in another publication (14).

Hytten and Leitch (13) estimated the increase in resting metabolism in pregnancy to be 26 400 kcal (111 MJ), and the energy value of tissues laid down in the fetus and placenta and in the reproductive organs of the mother to be about 12 500 kcal (52 MJ). A supplementary allowance of 40 000 kcal (167 MJ) would just cover these extra needs. On the other hand, Oldham and Sheft (15) observed that the maximum retention of nitrogen during pregnancy occurred with intakes of 36-40 kcal/kg (150-170 kJ/kg) of pregnant body weight per day, and in a more recent study King *et al* (16) reached a similar conclusion. Emerson *et al* (17) found only a slight net mean cumulative retention of nitrogen when the mean total metabolic cost of gestation was 27 120 kcal (114 MJ).

Because of these findings and of the danger of undernutrition of the fetus, a total additional intake of about 65 000 kcal (272 MJ) is recommended for pregnancy. Table II.3 shows how this amount is apportioned among the trimesters. If the intake of energy before pregnancy occurs is adequate and the weight gain during pregnancy is 10.5 kg, this amount is equivalent to an intake of 36 kcal/kg (150 kJ/kg)

of body weight per day, which is compatible with the observed intakes of normal pregnant women in the western world (8, 18).

A woman who gains 10.5-12.5 kg during pregnancy may be assumed to terminate it with an extra reserve of 2-4 kg of body fat, which can be used to supply energy for lactation. During a lactation period of 100 days, this reserve would yield 200-300 kcal/day (840-1300 kJ/day).

Lactation

A normal woman produces about 750 mL of milk per day, which is equivalent to 570 kcal (2400 kJ). Since the efficiency of human milk production is about 80% (19), the supplementary energy requirement for lactation is 710 kcal/day (3000 kJ/day). If 200-300 kcal (840-1300 kJ) comes from the woman's energy stores, 450 kcal (1900 kJ) should be supplied by the diet. The recommended supplement for lactation is therefore 450 kcal/day (1900 kJ/day), as indicated in Table II.3.

Children and Adolescents

As weight for height is the best index of the energy status of adults, normal growth and adequate weight for height are the most reliable indices of the adequacy of intakes of energy by children and adolescents. Growth curves for children of various ethnic backgrounds (20, 21) should serve this purpose.

In the planning of diets for groups of children, the results of surveys of food consumption can serve as a guide for the estimation of requirements for energy. The recommendations shown in Table II.1 are based on the results of such surveys that have recently been made in Canada (22-25). Because of differences in body size and activity and in rates of growth and development, the requirements vary even more among children than among adults. Caution must be used, therefore, in interpreting differences between observed intakes of a group of children and the average requirements.

In Table II.1 the age groups include three successive months in the first year of life, 2 years for the third and fourth, and thereafter 3 years up to age 19. The recommendations for children in the first year correspond approximately to the variations in the slope of the curve of intakes of energy relative to body weights that were found in recent studies (22-24). The 1-year interval between 1 and 2 years is justified by the direction of the change in intake per kilogram of body weight, an increase over the previous 6 months, and a rapid increase of 20-25% compared with the following 2 years. The percentage gain in body weight is similar during each year of the 3-year periods of the later years of childhood. There are differences in energy consumption between the sexes at an early age, and certainly from about 7 years onward (25, 26).

Table II.1. Average Energy Requirements[a]

Age	Sex	Average Height (cm)[c]	Average Weight (kg)[c]	Requirements[b] kcal/kg[c,d]	MJ/kg[d]	kcal/day[e]	MJ/day[f]	kcal/cm[g]	MJ/cm[f]
Months									
0-2	Both	55	4.5	120-100	0.50-0.42	500	2.0	9	0.04
3-5	Both	63	7.0	100-95	0.42-0.40	700	2.8	11	0.05
6-8	Both	69	8.5	95-97	0.40-0.41	800	3.4	11.5	0.05
9-11	Both	73	9.5	97-99	0.41	950	3.8	12.5	0.05
Years									
1	Both	82	11	101	0.42	1100	4.8	13.5	0.06
2-3	Both	95	14	94	0.39	1300	5.6	13.5	0.06
4-6	Both	107	18	100	0.42	1800	7.6	17	0.07
7-9	M	126	25	88	0.37	2200	9.2	17.5	0.07
	F	125	25	76	0.32	1900	8.0	15	0.06
10-12	M	141	34	73	0.30	2500	10.4	17.5	0.07
	F	143	36	61	0.25	2200	9.2	15.5	0.06
13-15	M	159	50	57	0.24	2800	12.0	17.5	0.07
	F	157	48	46	0.19	2200	9.2	14	0.06
16-18	M	172	62	51	0.21	3200	13.2	18.5	0.08
	F	160	53	40	0.17	2100	8.8	13	0.05
19-24	M	175	71	42	0.18	3000	12.4		
	F	160	58	36	0.15	2100	8.8		

Table II.1. Average Energy Requirements[a]

Age	Sex	Average Height (cm)[c]	Average Weight (kg)[c]	Requirements[b] kcal/kg[c,d]	MJ/kg[d]	kcal/day[e]	MJ/day[f]	kcal/cm[g]	MJ/cm[f]
Years									
25-49	M	172	74	36	0.15	2700	11.2		
	F	160	59	32	0.13	1900	8.0		
50-74	M	170	73	31	0.13	2300	9.6		
	F	158	63	29	0.12	1800	7.6		
75+	M	168	69	29	0.12	2000	8.4		
	F	155	64	23	0.10	1500	6.0		

[a] Data on children up to 3 years of age are based on references 22-24. Those on children of age 4 and up and on all adults are based on references 8-10, 25, 26.

[b] Requirements can be expected to vary within a range of ± 30%.

[c] Figures rounded to the closest whole number when ≥10 and to the closest 0.5 when <10.

[d] First and last figures are averages at the beginning and at the end of the 3-month period.

[e] Figures rounded to the nearest 50 when <1000 and to the nearest 100 when ≥1000.

[f] Figures include 2 decimals if value is <1 and 1 decimal if ≥1.

[g] Figures rounded to the nearest 0.5.

Table II.2. A Model of Energy Expenditure by a Young Adult Canadian

Type of Activity	Rate of Expenditure				Expenditure per Day					
	kcal/min		KJ/min		h/day		kcal		MJ	
	M[a]	F[a]	M	F	M	F	M	F	M	F
Resting metabolism	1.2	0.9	5.0	3.8	8	8	580	430	2.4	1.8
Sitting or standing still	1.6	1.2	6.7	5.0	10	11	960	792	4.0	3.3
Light activity[b]	3.2 (1.7-4.8)	2.5 (1.4-3.5)	13.4 (7.1-20.1)	10.5 (5.9-14.6)	4	4	770	600	3.2	2.6
Moderate activity[c]	5.6 (4.9-7.4)	4.5 (3.6-5.5)	23.4 (20.5-31.0)	18.8 (15.1-23.0)	2	1	672	270	2.8	1.2
Totals					24	24	2982	2092	12.4	8.8

[a] Male, Female.

[b] Walking slowly; light domestic work (*e.g.*, cooking, washing dishes, ironing, dusting, sweeping); light office or industrial work (*e.g.*, typing, laboratory work, sewing, printing, working with light tools); sports involving light activity (*e.g.*, golf, sailing, bowling).

[c] Walking at moderate speed; moderate domestic work (*e.g.*, scrubbing floors, cleaning windows, polishing furniture); moderate industrial work (*e.g.*, painting, plastering, modern farming); hobbies involving moderate activity (*e.g.*, gardening, woodworking, dancing); sports such as tennis, cycling, skiing, swimming, skating and jogging (for these the energy requirement is higher but they represent a small fraction of the total activity).

Table II.3. Additional Energy for Pregnancy and Lactation

	Additional Intake per Day	
	kcal	MJ
Pregnancy		
First trimester	100	0.4
Second and third trimesters	300	1.3
Lactation	450	1.9

When expressed in relation to body weight, figures for energy consumption in the first year of life are given as average intakes at the beginning and end of each 3-month period to indicate the direction of the change over that period. The total intake per day is based on an average for the period.

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III. CARBOHYDRATE AND FIBRE

The carbohydrates in food are primarily sugars, starches, hemicelluloses and cellulose, which have the empirical formula $C_n(H_20)_x$ with n greater than 4. The available carbohydrate in food is the portion that is digested and therefore made available for absorption and metabolism. This fraction includes glucose, fructose, sucrose, lactose, maltose, the higher malto series of oligosaccharides and the α-glucan polysaccharides (starches, dextrans, glycogen), some sugar alcohols and related substances. The unavailable portion of the carbohydrate in foods is the portion that is not hydrolysed by digestive enzymes, not absorbed, or if absorbed, not metabolized. This fraction includes the raffinose series of oligosaccharides, non-α-glucan polysaccharides (*e.g.*, cellulose) and some sugars (*e.g.*, lactulose). Although the definition of dietary fibre is controversial, it is generally accepted that it is composed of hemicellulose, cellulose, pectin and lignin. A recent FAO/WHO group (1) has defined dietary fibre as "the sum of lignin and polysaccharides that are not hydrolyzed by the endogenous enzymes of the gastrointestinal tract."

Carbohydrate is a major source of energy in the human diet, contributing approximately 40-80% depending upon the national diet of the country being considered (2). Recent estimates of energy from carbohydrate in the diet of Canadian adults give approximately 40% (3,4). The average for children is higher at 46-50% (3,5). At present there is no information on the composition of the carbohydrate in the diets of adults but estimates have been made for children in Ontario (5). It was found that children 5-17 years old obtained an average of 27% of their dietary energy from free sugars, namely (percentage of total energy) sucrose (15%), lactose (5.2%), fructose (2.6%), glucose (2.4%) and others (2.2%).

Carbohydrate is a substantial contributor to the energy value of most diets. It is very difficult, however, to estimate a dietary requirement for either total carbohydrate or its individual components.

A lower limit of intake has been argued on two grounds but neither is absolute. First, glucose is an essential energy substrate for the central nervous system, adrenal cortex and blood cells. These tissues utilize 100-150 g of glucose per day, but some can be provided by gluconeogenesis from amino acids, and furthermore, with time the brain can adapt to the use of ketones rather than glucose as an energy source. Ketosis and ketotic diets are not desirable, however, and ketosis can be prevented by intakes of carbohydrate of about 100 g/day (6). A second argument for a minimum level of one constituent of dietary carbohydrate, namely fibre, is often presented (1). Certain dietary fibres are recognized as playing an important role in the gastro-intestinal tract. Increased faecal bulk and slower absorption of digestible carbohydrate have been well documented. Other putative effects of dietary fibre such as prevention of the formation and action of carcinogens in the colon remain to be evaluated; but fibre may have the undesirable effect of reducing the bioavailability of certain minerals such as calcium, iron and zinc. These latter interactions have been suggested by the results of studies on experimental animals but there is much less convincing evidence from studies on humans (1).

An upper limit of carbohydrate consumption is similarly not clear although at least three observations are relevant. First, several carbohydrates, and particularly sucrose, influence the dental flora that through acid production causes dental decay. It is impossible, however, to state an absolute intake of simple sugars that is undesirable, because the physical form of the food and the frequency of eating, which influence the duration of time that the carbohydrate is available as a bacterial substrate, are as important as the chemical form (1). Second, the intake of carbohydrate, particularly of simple refined sugars, has been claimed to be a factor in the aetiology of obesity, cardiovascular disease and diabetes mellitus. There is no doubt that studies with the use of excessive amounts of certain carbohydrates such as sucrose, glucose or fructose have shown that metabolism can be distorted from that associated with a normal diet. The relevance of such information to variations in intake in usual Canadian diets, however, is not clear. There is no evidence that a change in the carbohydrate components of current Canadian diets would have any effect on the prevalence of obesity, cardiovascular disease or diabetes mellitus. Third, based on tests involving relatively large oral doses of lactose, hypolactasia has been described in significant proportions of the North American population, but it is still uncertain to what degree hypolactasia influences lactose digestion when the sugar is consumed in usual amounts in food. For this reason it is suggested that the use of milk for children should be discouraged only when there is clear clinical evidence of intolerance (1).

During the past 40 years the disappearance of sucrose from the Canadian food supply has remained relatively constant at about 15% of the total energy of the national diet (7), but the total carbohydrate, expressed as a proportion of the total energy, has declined. This appears to be due to the replacement of complex carbohydrates by fats. It would seem appropriate, in view of the putative benefits of dietary fibre and the circumstantial relationship of excess dietary fat to cardiovascular disease, to recommend that a part of the fat component be replaced by foods rich in complex carbohydrates, including fibre. This recommendation is consistent with previous guidance provided in nutrition recommendations for Canadians (8). That is, the Canadian population should be encouraged to increase the carbohydrate content of its diet, primarily from foods with a high content of complex carbohydrates and fibre, to at least 50% of the total energy value of the diet.

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IV. FAT AND ESSENTIAL FATTY ACIDS

Fat has several nutritional functions. It serves as a source of essential fatty acids, is a concentrated source of energy, acts as a carrier of fat soluble vitamins, contributes to satiety and affects the palatability of foods. The essential fatty acids are components of cell membranes and precursors of prostaglandins, thromboxanes, prostacyclins and leukotrienes.

Dietary fat is a mixture of lipids that includes triacylglycerides, phospholipids, cholesterol, phytosterols and fat soluble vitamins. Since over 95% of the fat in most diets is in the form of triacylglycerol, the characteristics of a dietary fat are largely determined by the nature and position of the fatty acids in triacylglycerides. Most saturated fatty acids contain straight even-numbered chains of 4 to 24 carbon atoms. Unsaturated fatty acids contain one or more double bonds, and those called polyunsaturated contain two or more double bonds. Most unsaturated fatty acids that occur naturally have a *cis* configuration that may isomerize to the *trans* form during partial hydrogenation. The physical and nutritional properties of *trans* unsaturated fatty acids resemble those of saturated fatty acids more than those of *cis* unsaturated fatty acids (1).

The principal essential fatty acid is linoleic acid, the parent of the n-6 family of polyunsaturated fatty acids, which are characterized by the last of their *cis* methylene interrupted double bonds being six carbons from the terminal methyl group. Linoleic acid can be metabolically desaturated to γ-linolenic acid, which in turn can be elongated to dihomo-γ-linolenic acid and then desaturated to arachidonic and docosapentaenoic acids. Dihomo-γ-linolenic acid is the precursor of the prostaglandin 1 series and arachidonic acid is the precursor of the prostaglandin 2 series (2).

A deficiency of essential fatty acids in experimental animals has been well described (3, 4). The signs include impaired efficiency of energy metabolism, excessive loss of water through the skin, scaly

skin, dermatitis, deranged kidney function, fatty liver from deposition of saturated and monounsaturated cholesteryl esters, abnormal electrocardiogram and reproductive failure in both sexes. A ratio of triene (20:3, derived from oleic acid) to tetraene (20:4, arachidonic acid) above 0.4 in serum lipids is, for most of the life span, an indication of deficiency of essential fatty acids (5).

Human infants deprived of essential fatty acids have developed skin eruptions, changes in serum lipids and an increased sensitivity to infection (6-9). The deficiency does not occur when linoleic acid provides 1% of the food energy. The linoleate content of human milk depends on the intake of the mother, and it varies greatly (10). Generally human milk contains about 5-10 times as much linoleic acid as cow's milk. An average value for the n-6 fatty acids of human milk is about 5% of the energy, and of the n-3 fatty acids about 1% of the energy (11). Infants fed cow's milk have a higher triene to tetraene ratio than those fed breast milk (4), indicating that the fat of cow's milk provides inadequate amounts of essential fatty acids and that other sources of them should be present in the diet. Substitutes for human milk should reflect its fatty acid pattern as closely as possible.

Adults show signs of essential fatty acid deficiency after prolonged parenteral feeding with preparations lacking fat (12-14). Normal values for the triene to tetraene ratio in the serum phospholipids of hospitalized patients with no metabolic disease and on typical North American mixed diets have been observed to be well below 0.4, with a mean value of approximately 0.1 (4).

α-Linolenic acid, 18:3, n-3, has been shown to relieve dermal symptoms but not other manifestations of essential fatty acid deficiency (15). Excitable tissues such as brain (16, 17) and retina (18) contain high concentrations of the long chain polyunsaturated fatty acids of the n-3 family; but in a study with rats that received low levels of linolenic acid over two generations, a specific deficiency of α-linolenic acid was not detected (19). A more recent observation on a growing girl who was parenterally fed a mixture containing a high level of linoleic but a negligible quantity of α-linolenic acid showed the development of neurological symptoms that were corrected by the administration of a preparation containing linoleic and α-linolenic acids in a ratio of 7:1 (20). Similar relative concentrations of n-6 and n-3 polyunsaturated fatty acids in the human fetus have been estimated to be 400 and 50 mg/kg of body weight respectively (21).

Since the conversion of linoleic to arachidonic acid may be hindered by the presence of linolenic acid (22), the dietary level of linoleic acid should be several times that of linolenic. The n-3 fatty acids have been implicated in reducing thrombogenesis, but their inhibitory effects on the synthesis of prostaglandins and other derivatives of arachidonic acid should be kept in mind (23).

The role of polyunsaturated fatty acids in lowering the level of serum cholesterol involves a higher intake than that associated with the prevention of symptoms of an essential fatty acid deficiency. Although many questions about dietary fats are unresolved (24), it is generally agreed that there is an association between a high intake of saturated fatty acids and a high level of serum cholesterol (25, 26). A reduction of fat within our present dietary pattern (27), in which more than half of it is in an unseparated or invisible form, would decrease the intake of saturated fatty acids. Linoleic acid is a constituent of a wide variety of foods of plant and animal origin and is in high concentration in some vegetable oils, and arachidonic acid occurs in animal membranes.

The total amount of fat in the diet must be related to the stage of development and to the requirement for energy. It supplies about half of the energy in human milk but less in the diet of the child after it is weaned. During growth, when the gastro-intestinal capacity is limited and the energy requirement is high, the intake of fat should be such that the energy density of the diet is adequate. A minimum level of 15% of energy from fat has been proposed for all age groups (11). Since fat is a concentrated source of energy (9 kcal/g (37 kJ/g)), a high proportion of it in the diet may jeopardize the intake of other nutrients, particularly when the total consumption of energy is low.

To ensure an adequate intake of essential fatty acids, it is recommended that they should provide 3% of the energy intake of children and adults. This level, recommended by a committee of the FAO and the WHO (11), refers to diets that contain appreciable amounts of other fatty acids, including saturated and *trans* unsaturated fatty acids. For pregnancy and lactation, additional intakes of energy are recommended; therefore more essential fatty acids should be available during the growth of the placenta and fetus and the production of milk. Recommended intakes of essential fatty acids are predominantly for linoleic acid.

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V. PROTEIN

The body does not have a requirement for protein *per se*. Rather, dietary protein serves as a source of amino acids required for the synthesis of tissue proteins. Proteins are made up of about 20 common amino acids of which 9 are considered to be essential and must be provided preformed. The others, termed the dispensable amino acids, can be synthesized in the body if a suitable source of amino groups (*e.g.*, other amino acids) is available. Both essential and dispensable amino acids are utilized in the synthesis of body proteins needed for accretion of new tissue (growth, pregnancy, lactation) and for the replacement of body proteins as they are normally broken down (protein turnover, maintenance requirement). Requirements for protein are estimated on the assumption that the supply of energy to the tissues (intake or mobilization of reserves from adipose tissue) is adequate. If it is not, the breakdown of protein is increased. At or near the level of requirement there is interaction between the requirements for protein and energy (1).

It is customary to consider protein requirements in terms of the total need for sources of nitrogen (total need for amino nitrogen) and of the need for specific essential amino acids. The latter influences what is commonly referred to as protein quality, which depends on both the concentration of amino acids in the dietary protein and its digestibility. Because individual dietary proteins vary in composition, an amino acid that may be in low concentration in one is often complemented by a higher level in another when the mixed sources of protein are consumed together (within a period of 12-24 h). It is very misleading to consider the quality of individual proteins in isolation because quality must be judged in the perspective of a mixed diet. Thus, although individual plant proteins often have a lower quality than animal proteins, mixed vegetarian diets, particularly those that include some milk, cheese and eggs, have an overall protein quality, in terms of the amino acids that they contain, that seems generally comparable to that of the mixed Canadian diet (2-6). It now seems clear that the adult is relatively insensitive to moderate differences in the amino acid composition of proteins as encountered in various mixed sources (7). Infants and young children are more sensitive to it. People of all ages are sensitive to differences in the digestibility of protein from different dietary sources.

Requirements and Recommended Intakes

An FAO/WHO committee considered protein requirements in 1971, reporting in 1973 (7). Since that time two supplementary statements of advisory groups based upon the recommendations have been published by these agencies (1, 8). This series of reports has been adopted as the basis of the present recommendations, with adjustment and modification to fit Canadian conditions.

Two approaches have been followed in predicting human requirements for protein. One is the direct measurement, in studies in metabolic wards, of the amount of dietary protein (of high quality) that must be ingested to maintain nitrogen balance (intake = total losses) in adults or to support satisfactory rates of protein accretion (positive nitrogen balance) in children. These are very time-consuming and very expensive studies, hence available data are limited. There is also reason to be concerned about the suitability of nitrogen balance as the best indicator of protein requirement, but at present no better one is available.

The second approach, often termed the factorial method, makes use of measurements of obligatory losses of nitrogen (urinary, faecal and dermal losses when the diet contains little or no protein), the expected increments to body nitrogen during growth and pregnancy and the secretion of nitrogen during lactation. Protein is then calculated as the amount of nitrogen multiplied by 6.25, since the average nitrogen content of most proteins is about 16%. The advantage of this approach is that the estimation of obligatory loss, at least in adults, can be made relatively easily, hence a more substantial volume of data is available.

When these two approaches were compared by the FAO/WHO committee (7), it was found that the factorial method substantially underestimated the amount of dietary protein necessary for nitrogen balance. Factorial estimates are based on losses at very low levels of intake; but as the intake increases toward the level of requirement, the efficiency of utilization of the dietary protein decreases (endogenous losses increase). It was therefore necessary to include an adjustment factor in the factorial approach to the estimation of dietary requirements. Originally these estimates were increased by a factor of 1.3. In a more recent review of the available data, it was suggested that although 1.3 is the appropriate factor for adjustment for infants and young children, it should be about 1.45 for adults (1). The authors of the review noted also that additional attention should have been given to the levels of energy intake in reported balance studies, although at that time no specific adjustments to estimated protein requirements were proposed. In the present report, attention has been directed to the

question of energy intake in balance studies and a new adjustment for the factorial prediction (1.7) is adopted.

Within the last few years it has become apparent that within the range of intakes that approximate requirements for energy and protein there is an important interaction between the intake of energy and the amount of protein required to establish nitrogen balance (1). If the energy intake is increased, the apparent protein requirement is decreased. The FAO/WHO review committee estimated that this effect might have a magnitude of about 0.04 g of protein per kilogram of body weight for each 1 kcal/kg (0.01 g/kg for each 1 kJ/kg) of change in the intake of energy near requirement levels if the most extreme situation is considered.

Early metabolic studies on requirements tended systematically to provide the subjects with too much energy, the assumption being that this would avoid recognized major effects of inadequacy of energy on the utilization of the protein, and as a result, they may have systematically underestimated protein requirements. Some recent trials, in which energy intakes were generally lower but thought to be adequate to meet the subjects' needs, have suggested that the FAO/WHO safe level of intake for the young adult may be low (1, 9-11) and indeed may approximate the average requirement rather than the average plus 2 standard deviations, as had been assumed. The underestimate may have been the result of both inappropriate adjustment to the factorial model (1.3 rather than 1.45) and the problem imposed by surplus energy intake in the studies on nitrogen balance serving as the primary indicator of requirement. Given the present uncertainties, the protein requirement of the average adult male is taken as 0.57 g/kg/day, the old FAO/WHO safe level of intake of egg or milk protein. This is based on observed nitrogen balance data (1,9-11). This level is 1.7 times that predicted by the original factorial model of nitrogen losses. The factor 1.7 is applied for adults in deriving the recommended intakes in Table V.1.

The above modification from the FAO/WHO report refers to adults. The estimates of requirements for infants were based upon direct studies of intakes that have not been challenged and are accepted as valid. The adjustment in the factorial model for infants remains at 1.3. It is assumed that between infancy and adulthood the required adjustment in the factorial model progressively increases from 1.3 to 1.7. Although there are no data to confirm this assumption directly, the recommended amounts were calculated by increasing the factor for adjustment in linear proportion to age from 1 to 20 years.

The factorial estimate of the average requirement for nitrogen represents the summation of predicted obligatory losses and the simulated rate of accretion for each age period. To extrapolate from figures

for adults to those for children, it was assumed that obligatory losses were related to the basal metabolic rate, and were taken as 2 mg of nitrogen per basal kilocalorie (0.5 mg per basal kilojoule) (7). This may be somewhat of an overestimation of the actual losses by infants and young children. Recent studies suggest that it may somewhat underestimate the losses of adults (1), which is taken into account in the correction factor discussed above. Since 1971, studies on elderly people and on women have given general support for the average estimates of requirements made at that time (7), with moderate adjustment (1). In the present report, no adjustment of protein requirement per kilogram of body weight is made for adults after the age of 25. The application of progressive adjustment factors between infancy and adulthood is illustrated in Table V.1.

The average requirement is increased by 30% to allow for individual variability, which assumes a coefficient of variation of about 15%. The 1971 committee derived this figure from several types of observation: the variability of obligatory excretion of urinary nitrogen (the major component of the factorial model), the apparent variability of growth rate and, in pregnancy, the variability of birth weight (7). Although the observed variability of protein requirement in nitrogen balance studies was higher than this, it was suggested that it was increased by experimental variation (7). This estimate of variability was assumed to take into account minor stresses of daily living but not necessarily increases that might be associated with serious infections, etc. These adjustments provide an estimate of the recommended intake expressed in terms of egg or milk protein, which must then be adjusted to take into account the nutritional quality of the mixed dietary protein.

Adjustment for Quality

Adjustment for qualilty of the protein may be made on the basis of the chemical composition of the average diet or of the biological utilization of mixed dietary proteins, as measured in studies on animals (7). With either approach, the evaluation of quality must be relative to that of the protein of milk or egg since they are the proteins of high quality used for purposes of defining reference protein requirements.

In Table V.2 a comparison is made of the reanalysed apparent amino acid composition of the mixed protein disappearing in the Canadian food supply (6) with the provisional pattern suggested by the FAO/WHO committee (7). The apparent limiting amino acids are either the sulphur amino acids or threonine, and the predicted chemical score is about 95%. If it is assumed that the digestibility of the mixed protein is about 90% in comparison with that of egg or milk, the appropriate correction factor for the nutritional quality of the Canadian dietary protein is (100/95) × (100/90) = 1.17. In animal studies,

Table V.1. Derivation of the Recommended Intakes of Protein

Age	Sex	Factorial Estimate of Average Nitrogen Requirement: Growth and Obligatory Loss (FAO/WHO)[a] (mg/kg per day)	Adjustment of Factorial Estimate to Accord with Observed Nitrogen Balance Data[b]		Recommended Intake of Egg or Milk Protein[d] (g/kg per day)	Recommended Intake of Canadian Dietary Protein	
			Factor	Average Protein Requirement[c] (g/kg per day)		Factor to Adjust for Quality	(g/kg per day)
Months							
0-2	Both				2.40	1.0	2.4
3-5	Both				1.85	1.1	2.0
6-8	Both	154	1.3	1.25	1.63	1.2	2.0
9-11	Both	136	1.3	1.11	1.44	1.3	1.9
Years							
1	Both	120	1.32	0.99	1.29	1.3	1.7
2-3	Both	109	1.34	0.91	1.19	1.3	1.5
4-6	Both	96	1.40	0.84	1.09	1.26	1.4
7-9	M	84	1.46	0.76	1.00	1.23	1.2
	F	84	1.46	0.76	1.00	1.23	1.2
10-12	M	76	1.52	0.72	0.94	1.20	1.1
	F	73	1.52	0.69	0.90	1.20	1.1
13-15	M	68	1.58	0.67	0.87	1.17	1.0
	F	59	1.58	0.58	0.75	1.17	0.89

Table V.1. Derivation of the Recommended Intakes of Protein

Age	Sex	Factorial Estimate of Average Nitrogen Requirement: Growth and Obligatory Loss (FAO/WHO)[a] (mg/kg per day)	Adjustment of Factorial Estimate to Accord with Observed Nitrogen Balance Data[b]		Recommended Intake of Egg or Milk Protein[d] (g/kg per day)	Recommended Intake of Canadian Dietary Protein	
			Factor	Average Protein Requirement[c] (g/kg per day)		Factor to Adjust for Quality	(g/kg per day)
Years							
16-18	M	58	1.64	0.59	0.77	1.14	0.88
	F	53	1.64	0.54	0.71	1.14	0.81
19-24	M	54	1.70	0.57	0.74	1.10	0.82
	F	49	1.70	0.52	0.68	1.10	0.74
25+	M	54	1.70	0.57	0.74	1.10	0.82
	F	49	1.70	0.52	0.68	1.10	0.74

[a] Reference 7.
[b] References 1, 9-11.
[c] N × 6.25.
[d] Average × 1.3 to allow for individual variability of need.

the net protein utilization from diets formulated to contain the approximate average mixture of proteins in the Canadian diet is 67 (6). The reported net utilization of the protein of egg or milk, the reference standard, is about 90 (7). In consideration of these two estimates, for the present report it was accepted that for young children a factor of 1.3 would be appropriate to adjust for the quality (amino acid composition and digestibility) of the protein in the usual mixed Canadian diet. On the basis of these considerations, an adjustment factor of 1.3 was adopted. As noted earlier, mixed vegetarian diets as consumed in Canada do not seem to have a distinctly different amino acid composition or require a distinctly different adjustment factor. The use of this factor may give a somewhat low estimate of the dietary needs for protein of children eating strictly vegetarian diets, particularly if they are based principally on cereals or are very restrictive in types of foods.

Table V.2. Amino Acid Composition of the Average Mixed Protein in the Diet of Canadians

	Amino Acid Pattern, mg/g Nitrogen	
Amino Acid[a]	Canadian	FAO/WHO Provisional Pattern
Isoleucine	292	250
Leucine	495	440
Lysine	385	340
Phenylalanine + Tyrosine	511	380
Methionine + Cystine	213	220
Threonine	240	250
Tryptophan	77	60
Valine	360	310

[a] Histidine is also required by the infant and perhaps by the adult but is not thought to be limiting in the mixed proteins in the Canadian diet.

In the derivation of these recommendations, the adjustment factor for quality was not used uniformly across all ages. In the case of very young infants, it was assumed that the protein ingested would be derived from breast milk or formulae containing protein of high biological value, so no adjustment for quality was required. For older infants, it was assumed that other sources of protein would be introduced into the diet gradually, with consequent lowering of the quality, so the adjustment factor was progressively increased from 1.0 at the end of 3 months to 1.3 after 12 months, as shown in Table V.1.

The FAO/WHO committee that reported on protein requirements in 1965 (12) recognized that sensitivity of requirement to differences in quality of the protein decreases with increasing age up to adulthood. That committee discussed the question in terms of the required ratio of essential to total amino acids (E/T ratio) and pointed out that in many situations, particularly for the adult, it is likely to be the total supply of amino acids rather than the specific supply of essential amino acids that determines the dietary requirement for protein. It has been demonstrated, for instance, that the need for high quality protein can be reduced if there is a source of dispensable amino acids (the E/T ratio can be lowered without affecting the protein requirement). The 1973 report (7) again referred to this issue and noted that the suggested correction factor for quality is likely to give an overestimate of the actual requirements of adults. That committee attempted to describe the amino acid requirements of infants, of schoolchildren in the 10-12 age group and of adults. From these the E/T ratios may be calculated as (histidine omitted): infant, 0.36; 10-12 years old, 0.32; adult, 0.15. The final provisional pattern of amino acids was that appropriate for an infant or a young child, and had an E/T ratio of 0.36.

The implication of this is that an effect of amino acid composition on the dietary protein requirement of the adult should not be expected unless the amino acid score is below about 42% ((0.15/0.36) × 100) of that of egg or milk protein. Experimental trials have not demonstrated that egg protein can be diluted with dispensable amino acids to that degree, but it has been confirmed that adults are relatively insensitive to the quality of the dietary protein if it is measured in terms of its amino acid composition. The 1971 committee (7) reviewed nitrogen balance studies in which adults had consumed various sources of protein and found that with diets in which part of the protein was from animal sources, the nitrogen requirement was only slightly above that in egg or milk protein. When single sources of protein of plant origin or mixed diets of plant materials based heavily on cereals were eaten, the nitrogen requirement was increased by 20%. These effects are what might be expected from consideration of the digestibility of such diets without regard for differences in amino acid composition. For adults, it may be assumed that for mixed diets the only correction needed is for digestibility. In the case of the Canadian mixed diet, this is taken as 90% relative to egg or milk protein and the figure to adjust for quality is set at 1.1 for adults.

Examination of the figures for children 10-12 years old that were used in 1971 shows that the apparent E/T ratio is 0.32, about 89% of that of the provisional amino acid pattern (7). This would suggest that children in this age group are less sensitive to protein quality than are infants, but more sensitive than adults. It seems probable that the

experimental design may have led to an overestimate of amino acid requirements at this age and hence a prediction of greater sensitivity than actually exists; but for present purposes, the estimate is accepted.

In the derivation of the figures for recommended intakes, the correction factor for protein quality has been progressively decreased from 1.3 at age 4 to 1.1 at age 19, which reflects a progressively decreasing sensitivity to the amino acid composition of the mixed dietary protein but maintains recognition that its digestibility affects its utilization in all age groups (Table V.1). Within age and sex groups, the recommended intakes may be adjusted on the basis of body weight. In all probability the true variable is lean body mass. In obese subjects a simple adjustment for body weight may overestimate the actual requirements.

It will be recognized that the recommended intakes are below the usual dietary intakes of most Canadians, but there is no implication that these customary intakes should be lowered to the levels of the recommendations, which are meant to describe intakes at which there is a low risk of inadequacy (to maintain nitrogen balance or provide for expected nitrogen accretion) for the individual. They are not statements of optimal intakes but of the lower limits of safe ranges of intakes.

Pregnancy and Lactation

The factorial approach to the estimation of protein requirements in pregnancy makes use of a model of tissue composition and protein accretion published by Hytten and Leitch (13), which predicts the average rates of accretion of protein shown below.

Stage of Pregnancy	Average Rate of Accretion of Protein (g/day)
First Quarter	0.5
Second Quarter	2.5
Third Quarter	4.6
Fourth Quarter	5.4

In the construction of this model, the weight of the infant at birth was seen as a major determining variable. Since birth weight is reported to have a coefficient of variation of about 15%, this was taken as a first approximation of the variability of the protein requirement in pregnancy (7). This estimate of protein need derived from the factorial model is generally regarded as a conservative one.

It is difficult to interpret nitrogen balance studies during pregnancy since, unlike the situation in the non-pregnant adult, equality of intake and excretion cannot be expected because the normal pregnant

woman should be in positive nitrogen balance. In long-term studies of nitrogen balance during pregnancy, it has been observed that the apparent retention of nitrogen may be much higher than would be expected from the factorial model described above (14). Indeed, it appears that if the intakes of protein and energy are progressively increased during pregnancy, the retention of nitrogen also increases without a definable maximum, albeit accompanied by a progressive fall in the efficiency of utilization of the dietary protein. A serious theoretical problem is posed by our inability at present to account for the apparent additional nitrogen retention in terms of recognized increments in maternal tissues.

Calloway (14), reviewing published studies, reported an average retention of about 1.6 g of nitrogen, or 10 g of protein, per day in the second half of pregnancy, a value that is twice as high as that suggested by the model of tissue deposition of Hytten and Leitch (13). King *et al* (15), using diets that provided about 100 g of protein per day, observed average retentions of nitrogen equivalent to 13.4 g of protein per day in the last 6 weeks of gestation. Retentions of the order of 1.5 g of nitrogen per day have been obtained on much lower intakes than this (16).

In view of the uncertainty involved in the interpretation of the factorial model for pregnancy, and to err on the side of safety, the assumption is made that the mean retention of protein in late pregnancy is about 10 g/day, that the variability of the protein requirement is similar to that of birth weight (15%) and that the efficiency of utilization and sensitivity to quality for the pregnant woman are comparable with those for the non-pregnant adult. On this basis, the increase in the recommended intake would be $10 \times 1.7 \times 1.3 \times 1.1 =$ 25 g of mixed dietary protein per day during the last trimester. The need would be expected to be less in early pregnancy, although nitrogen balance studies in animals and man have suggested that protein may be deposited in the body in anticipation of later needs. The recommended intake for the first trimester is 15 g/day and for the second trimester 20 g/day as additions to the recommended amounts for the nonpregnant woman of the same age and the same weight before pregnancy.

The nitrogen content of breast milk varies with the stage of lactation (17). Although not all of the nitrogen is in protein and amino acids (17), it may be so considered for the purpose of estimating requirements. The nitrogen content of mature breast milk is about 200 mg/100 mL. An average daily secretion of 750 mL therefore provides about 9.4 g of protein. If the coefficient of variation of requirement is accepted as 15% and the efficiency of utilization and sensitivity to quality of the protein are taken as similar to those in the case of the non-pregnant adult, the additional requirement for lactation would be $9.4 \times 1.7 \times 1.3$

× 1.1 = 22.8 g of protein per day, an amount slightly lower than that suggested for late pregnancy. The recommended additional intake is 20 g/day. In early lactation, when the nitrogen concentration of the milk is higher, the volume is lower, so it is considered that the same recommendation is appropriate for all stages of lactation. It involves an addition to the amount recommended for a non-pregnant, non-lactating woman.

Effects of High Intakes

As well as serving as a source of amino acids for the synthesis of tissue proteins, dietary protein and amino acids are sources of energy (approximately 4 kcal/g (17 kJ/g)). Under normal conditions, the human body seems capable of metabolizing much higher intakes of protein than the amounts recommended in this report without apparent detrimental effect. As with other sources of energy, an increase in the proportion of protein in the diet may affect the requirements for other nutrients (*e.g.*, an increase in the requirement for vitamin B_6; and there may be an effect on calcium metabolism). The real upper limit of the safe range of intake would appear to be set by the body's ability to excrete the end products of the metabolism of protein, notably urea, which in turn depends upon the adequacy of the intake of water and upon kidney function. In normal subjects, the only practical risk, possibly in association with marginal immaturity of the development of kidney function, may be encountered in the feeding of infants if very high intakes of protein are provided in a formula with limited fluid volume.

It is again emphasized that under usual Canadian conditions, observed intakes of protein are above the recommended intakes but below the levels that might be cause for concern about excessive intakes. Thus, the usual dietary intakes of protein in Canada can be considered as well within the safe range.

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VI. FAT-SOLUBLE VITAMINS

Vitamin A

Vitamin A has primary roles in vision, in the maintenance of epithelial tissue, in bone growth and in reproduction. Except for its role in vision, in which retinaldehyde forms the prosthetic group of the visual pigments, the biochemical action of vitamin A is poorly understood (1).

Deficiency of vitamin A results in follicular keratosis and night blindness (2-4). In young children, severe deficiency has particularly disastrous effects upon the eye. The conjunctiva becomes dry, keratinized and infected, resulting in the condition of xerophthalmia, which frequently causes partial or total blindness (5). In spite of the fact that vitamin A was the first vitamin to be discovered and that it was shown by McCollum in 1913 to be necessary for the prevention of xerophthalmia in rats (2), vitamin A deficiency is still a significant cause of blindness among young children in some developing countries (5).

Vitamin A activity in food is contributed by the preformed vitamin, retinol, and provitamins A, carotenes (1, 6). During digestion the carotenoids are converted to retinol by enzymatic cleavage in the mucosal cells of the intestine (6). From there the retinol is absorbed into the lymphatic system as retinyl esters and transported to the liver where it is stored. These stores in the liver provide a reserve from which the vitamin may be mobilized as needed by the tissues. The retinol is mobilized from the esters, then released into the blood in a complex with a retinol binding protein and transported to the target tissue (7). As long as there are reserves in the liver, concentrations in the serum are maintained at a fairly constant level (1, 8).

The Vitamin A Content of Diets

Preformed vitamin A is present, primarily as retinyl esters, in animal products such as liver, kidney, eggs and milk. Carotene pigments that have provitamin A activity are abundant in fruits and vegetables. With respect to provitamin activity, the most important are

α- and β-carotene and cryptoxanthin. Certain synthetic food pigments, carotenals and carotenoic acid, also act as provitamins A (9).

As in the revised edition of the Dietary Standard for Canada published in 1975 (10), intakes of vitamin A are expressed in terms of retinol equivalents (RE), derived by the use of conversion factors suggested by an FAO/WHO expert group (11). The conversion factor for provitamin A is based on the assumption that one-third of ingested carotene is absorbed and that the efficiency of conversion of absorbed β-carotene to retinol is 50%. Other carotenes are assumed to have one-half the potency of β-carotene. Thus 1 RE corresponds to a biological activity in man of 1 μg of retinol, 6 μg of β-carotene or 12 μg of other carotenes.

Formerly it was customary to express the potency of vitamin A in international units (IU). According to this convention, 1 IU was provided by 0.3 μg of retinol or 0.6 μg of β-carotene, these values being based on the results of experiments with rats. This conversion, however, overestimated the availability to man of the provitamin relative to that of retinol, since, as indicated above, the efficiency of absorption of carotene is approximately one-third. Thus, for man, 1 RE is equivalent to 3.33 IU of activity from retinol or 10 IU from βcarotene. To translate international units of vitamin A into retinol equivalents and micrograms of retinol or β-carotene into retinol equivalents, the following formulae are used (8).

$$RE = (IU\ retinol)/3.33 + (IU\ \beta\text{-carotene})/10$$

$$RE = \mu g\ retinol + (\mu g\ \beta\text{-carotene})/6$$

Although there may be traces of provitamins in animal products, and other carotenes may occur with β-carotene in fruits and vegetables (11), when dietary vitamin A values are calculated it may be assumed that animal products contribute only retinol and plant products only β-carotene.

On the basis of food supplies available for consumption in Canada, two-thirds of the total vitamin A activity (RE) is provided as the preformed vitamin and one-third as provitamin carotenes (10).

Requirements

The literature to 1972 on vitamin A requirements has been reviewed by Rodriguez and Irwin (12). The problem of determining requirements has been complicated by the lack of sensitive criteria for evaluating vitamin A status and inability to estimate the magnitude of liver stores in living persons.

The carefully controlled study on human deprivation of vitamin A by the Medical Research Council (3) led to the conclusion that 1300 IU (390 μg of retinol) was the minimum protective intake per day for adults, although not for maintenance for blood levels of the vitamin,

and that 2500 IU (750 μg of retinol) per day would provide a margin of safety and presumably permit some liver stores. More recently, controlled studies with labelled retinol on adult males have indicated that 600 μg/day is sufficient to correct eye changes and skin lesions resulting from deprivation of vitamin A (4). With intakes of 600 μg of retinol per day, plasma levels were above 20 μg/100 mL, the minimum level associated with liver storage. Intakes of 1200 μg of retinol per day maintained plasma levels above 30 μg/100 mL (4).

Recommended Intakes

The recommended intake of vitamin A should be sufficiently above the minimum requirement to accommodate the considerable variation in rates of utilization among individuals (4) and to permit maintenance of a reserve in the liver (11). Because of their smaller body size, it is reasonable to assume that the needs of women are less than those of men.

A recommendation of 1000 RE/day is made for the adult man and of 800 for the adult woman.

For infants, the amount of vitamin A provided by breast milk from a well-nourished mother is considered sufficient. Reported amounts of vitamin A in human milk have generally fallen within the range 40-65 RE/100 mL (13-15). The recommended intake for infants is 400 RE/day.

There are few data other than those from nutrition surveys and status studies on the requirements of children for vitamin A (12). Recommended intakes (RE) per day are made in part proportional to body weight and include arbitrary amounts for growth. These are 400 for the age range 1-4 years, 500 for 4-7 years, 700 for 7-10 years, 800 for 10-13 years, 900 for boys and 800 for girls of 13-16 years and 1000 for boys and 800 for girls of 16-19 years (the same as for adults).

The vitamin A requirement of the woman is increased in pregnancy to meet the demands of maternal reproductive tissues and of the fetus and to provide for limited storage of the vitamin in the fetal liver. There is little firm information, however, on which to base the estimation of a requirement (12). Placental transfer of vitamin A to the fetus is limited and the rate appears to be homeostatically controlled (12). Greater fetal reserves may result from increased maternal intake (2), but whether this is desirable or necessary is not known (12). Levels of vitamin A in the livers of four stillborn Canadian infants averaged 38 μg of retinol per gram (16). On the basis of a liver weight of 150 g (17), this would amount to 5700 μg of retinol as a reserve. It is considered that the needs of the pregnant woman will be met by an additional 100 RE/day; therefore, the total recommended intake for the pregnant woman is 900 RE/day.

During lactation the intake of vitamin A should be increased by a

sufficient amount to cover that lost in the milk, about 400 RE/day (13-15). A total intake of 1200 RE/day for the lactating woman is therefore recommended.

Excessive Intakes

Excessive intakes of retinol are toxic. Symptoms of toxicity include desquamation of the skin and mucous membranes, abnormal hair growth, pain and tenderness in the long bones, headache, irritability, anorexia and fatigue (1, 2, 18, 19). Studies on animals have shown that an excessive intake during pregnancy is teratogenic (20). The appearance of toxic symptoms is a function of the amount and the duration of the intake. A review of several cases of vitamin A toxicity in children and adults led to the conclusion that symptoms appear when the amount in the liver exceeds 10 times the normal level (18).

The level of intake of vitamin A that is potentially hazardous varies with the form and source of the vitamin. Provitamins A are not toxic, although the consumption of large amounts of β-carotene may result in a yellowish discolouration of the skin (2). Usual intakes of preformed vitamin A in food are unlikely to be sufficiently high to cause toxicity (6); but the consumption of liver from some animals, e.g., the polar bear, seal and shark, which contain very high levels of retinol, has been associated with acute hypervitaminosis A (2, 18). The major potential hazard from vitamin A toxicity is that posed by potent pharmaceutical sources. Aqueous emulsions of retinol are more toxic than oily solutions (18). Toxic symptoms have been reported from continued daily doses of 40 000 IU (12 000 RE) and 50 000 IU (15 000 RE) by adults and of 25 000 IU (7500 RE) by a child (19, 21, 22).

In view of the potential adverse effects of excessive intakes of vitamin A it is essential that dietary supplements containing it be used with caution.

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Vitamin D

There are two nutritionally important forms of vitamin D as well as analogues derived from these parent compounds: cholecalciferol (D_3), the form synthesized by mammals, and ergocalciferol (D_2), the form widely used in pharmaceutical preparations. The natural precursor of vitamin D_3 is 7-dehydrocholesterol, which is converted to previtamin D_3 when the skin is exposed to ultraviolet radiation and then to vitamin D_3 by a slow thermal reaction that occurs mainly in the deep layers of the irradiated skin (1). When the skin is regularly exposed to sunlight, the entire requirement for vitamin D can be met by the endogenous synthesis of vitamin D_3. The amount of exposure to sunlight and thus the requirement for the vitamin is affected by geographic, climatic and cultural factors, and there is evidence that the pigmentation of the skin may affect the endogenous synthesis of vitamin D.

The important dietary sources of vitamin D in Canada include several marine oils and fish tissues, a few foods derived from animals, such as liver, eggs and perhaps meat from animals fed vitamin D supplements, and fortified milk and margarine (the major sources for most people). The results of recent studies with a relatively non-specific chemical assay suggesting that bovine and human milks contain nutritionally significant concentrations of a water soluble conjugate of vitamin D and sulphate (2) have not been confirmed by bioassay (3) or by chromatographic analysis (4). Metabolites of vitamin D, particularly 25-hydroxycholecalciferol, are the important antirachitic sterols in human and bovine milk (5). Current information indicates that the antirachitic activity of human and unfortified cow's milk ranges from 15 to 40 IU/L depending upon the intake of vitamin D from natural and supplementary sources.

The metabolism of vitamin D has been elucidated during the past decade. Cholecalciferol is converted by the liver to 25-hydroxycholecalciferol that in turn is converted in the kidneys to 1,25- and 24,25-dihydroxycholecalciferol. In the mammal, the same organs convert ergocalciferol to analogous derivatives with the same physiological activity and potency. The dihydroxy metabolites regulate, in the manner of hormones, the absorption, excretion and turnover of calcium (6) and, less importantly, of phosphorus (7).

Deficiency of vitamin D causes primarily a breakdown of calcium homeostasis. This results in a compensatory increase in the activity of the parathyroid glands that in turn alters phosphate homeostasis and causes hypophosphataemia and generalized aminoaciduria (8). The

blood may contain abnormally low levels of calcium, and affected infants are prone to develop convulsions and tetany, often before conspicuous skeletal changes occur. In children the deficiency disease is known as rickets, the symptoms of which include skeletal deformities, costochondral beading and bow legs. In adults, deficiency causes osteomalacia, in which the bones are rarefied, weakened and sometimes deformed.

These deficiency diseases have a variety of nutritional and socioeconomic roots. Historically, rickets has tended to appear when changes in life-style and environment have resulted in reduced exposure to sunlight (9). In industrial countries vitamin D deficiency was once a relatively common disorder (10). In North America the incidence of deficiency was dramatically reduced when some common foods were enriched with vitamin D (11). This practice is evidently necessary in northern latitudes where many people are confined indoors or heavily clothed in winter. In Canada, fortification of milk and margarine is authorized under the Food and Drugs Act. When people eat reasonable amounts of such foods, dietary rickets is not seen.

In Canada, overt vitamin D deficiency is now limited almost entirely to infants. Its occurrence can nearly always be linked to the absence of fortified milk (and of pharmaceutical supplements) from the diet (12). The majority of infants with vitamin D deficiency are breastfed or are being fed vegetarian or so-called natural diets from which fortified milk is omitted (13).

It is not feasible to try to measure requirements for vitamin D because of the factor of endogenous synthesis. It is known that at the tissue level the vitamin is required at all ages. It is known also that for infants born in the autumn, who would be expected to be exposed to very little sunlight, as little as 2.5 μg (100 IU) of vitamin D per day are sufficient to heal the biochemical and radiographic lesions of rickets. Experience over several decades has shown that an intake of 10 μg (400 IU) per day will prevent rickets, promote normal growth and maintain normal calcium and phosphorus homeostasis without toxicity, even in infants not exposed to sunlight (11). This level of intake certainly exceeds the requirements of infants. The levels ingested in breast milk are much lower than this. Only a very small proportion of breastfed infants who are not given supplements develop deficiency of vitamin D. It seems probable that the widely accepted figure of 10 μg (400 IU) per day considerably exceeds the true requirement of the great majority of infants, but that amount can be recommended as an effective and safe prophylactic level of intake from all sources.

There is very little information about the magnitude of vitamin D requirements beyond infancy. According to the Nutrition Canada survey (14), a considerable proportion of a representative sample of

both children and adults receive less than 100 IU/day from dietary sources, and by biochemical and clinical criteria there was virtually no deficiency. The observed intakes must be assumed to be adequate for most subjects given the usual levels of exposure to sunlight in this country.

On the basis of these considerations, the recommended intake for full-term normal infants up to 2 years of age is 10 μg (400 IU) per day as either cholecalciferol or ergocalciferol or biologically equivalent amounts of the active metabolites of vitamin D.

For almost all older children and adults it is accepted that the requirements for vitamin D can be met by casual exposure to sunlight and ingestion of the mixed Canadian diet. The recommended intakes are 5 μg (200 IU) per day for children up to 7 years and 2.5 μg (100 IU) per day for those beyond that age.

There is probably an increase in the requirement for vitamin D during pregnancy and lactation. The recommended intake during these periods is 5 μg (200 IU) per day.

These recommended amounts can be obtained by the ingestion of a reasonable diet that includes fortified milk or margarine.

Vitamin D in large doses is toxic. Excessive intake has been implicated as the cause of infantile hypercalcaemia (15). The results of surveys suggest that in the past some Canadian infants and children probably ingested undesirably large amounts when a multiplicity of fortified foods as well as high potency supplements were available (11). To guard against excessive intake, it is recommended that the total amount of vitamin D ingested from all sources by infants and by pregnant and lactating women should not greatly exceed the recommended amounts.

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Vitamin E

Vitamin E consists of two families of four naturally occurring compounds, the tocopherols and the tocotrienols (1). The members of each family are designated α, β, γ or δ depending upon the number and position of methyl groups attached to the chroman nucleus. In the tocopherols, the side-chain is saturated, and in the tocotrienols, unsaturated.

α-Tocopherol is the vitamer of greatest nutritional importance because of its widespread distribution and high biological activity, but the intake of γ-tocopherol is about three times that of α-tocopherol because of its predominance in many vegetable oils, margarines and shortenings (2). Hence γ-tocopherol, despite its lower biological activity, makes a significant contribution to the total vitamin E of the diet. The tocotrienols occur in certain cereal grains (*e.g.*, wheat, barley, oats) but probably have little nutritional significance. High performance liquid chromatography makes possible the separation and quantification of the various natural forms of vitamin E in foods (3). Synthetic

isomers of α-tocopherol are used as food supplements, the most frequently used being all-rac-α-tocopherol, also called *dl*-α-tocopherol, and its acetate ester.

The occurrence of several forms with different biological potencies has created a need for a common unit to express the vitamin E activity of foods and mixed diets. In the past a unit based on the activity of 1 mg of synthetic 2-*ambo*-α-tocopheryl acetate (isomeric at carbon 2) has been used as the international standard; but this standard is no longer available and consequently the international unit is now based on 1 mg of all-rac-α-tocopheryl acetate (isomeric at carbons 2, 4 and 8), which appears to have the same biological activity as the original standard. The activities assigned to the ester and to the corresponding *d*-isomers are as follows (IU/mg): all-rac-α-tocopherol, 1.1; *d*-α-tocopheryl acetate, 1.36; *d*-α-tocopherol, 1.49. Alternatively, biological activity is expressed in terms of *d*-α-tocopherol equivalents. This is the system used in the present recommendations. Relative to *d*-α-tocopherol, γ-tocopherol is assumed to have a potency of 0.1 (4). β-Tocopherol and α-tocotrienol, which may make a small contribution to dietary vitamin E under some circumstances, have potencies of about 0.5 and 0.3 respectively. Differences in activity among the various isomers appear to be due primarily to differences in retention times in the body.

The requirement for vitamin E is determined primarily by the concentration of polyunsaturated fatty acids (PUFA) in the tissues (5), and therefore varies significantly with the PUFA content of the diet. This relationship arises from the metabolic role of the vitamin as an antioxidant. Attempts to define the amount of vitamin E required in the diet in terms of a fixed ratio to the amount of PUFA consumed have met with difficulty since the ratio appears to change with the PUFA intake (6). With the amounts of PUFA in usual mixed diets, a ratio of 0.4 mg of *d*-α-tocopherol per gram of PUFA has been found satisfactory for both children (7) and adults (5), and this appears to be typical of a mixed diet in the United States (2). An evaluation of the distribution of vitamers in the American diet has indicated that compounds other than α-tocopherol (mainly γ-tocopherol) contribute about 20% to the total biological activity (2). Allowance for γ-tocopherol therefore raises the ratio to nearly 0.5 mg of *d*-α-tocopherol equivalents per gram of PUFA. The α-tocopherol content of the Canadian diet is increased by the use of rapeseed oil, which contains a higher concentration of α-tocopherol than does soybean oil. Analysis of a composite diet representative of the daily *per capita* consumption of foods in Canada yielded a mean α-tocopherol:PUFA ratio of 0.58 (8), and the degree to which this would be raised by inclusion of γ-tocopherol is uncertain. In general, however, there are no signs of vitamin E deficiency in the

Canadian population, which suggests that the relative amounts are adequate.

Most plasma levels of vitamin E in adults who eat a mixed diet fall within a range of 0.5-1.5 mg/100 mL. Typically, 10-15% consists of γ-tocopherol (9). There is a tendency for the plasma concentration to rise with that of cholesterol during adulthood since both are bound to similar lipoproteins. The plasma level of vitamin E therefore is frequently expressed in relation to that of lipoprotein or total lipid. Erythrocytes exposed to a mild oxidizing agent such as hydrogen peroxide are haemolyzed when the concentration of vitamin E in the plasma falls below 0.5 mg/100 mL. Hence this level has been proposed as the minimum desirable concentration in adults.

The Nutrition Canada survey found no evidence of a deficiency of vitamin E in the national population on the basis of serum levels but values were somewhat lower in Inuit and Indians than in the national sample (10, 11). This was also true of cholesterol, and may reflect a difference in lipoprotein concentrations. A study on three populations of young adult Indians in western Canada (12) revealed that one population had a mean plasma level of vitamin E (0.61 mg/100 mL) below those of the others and that of the national population. Plasma vitamin E was positively correlated with plasma cholesterol and with age. Two surveys on adults living in Ottawa and Vancouver yielded values generally within the normal range (13, 14).

Low plasma levels of β-lipoprotein, cystic fibrosis and biliary atresia are associated with low plasma levels of vitamin E.

Vitamin E in the plasma of term infants fed breast milk rises rapidly from an initial value of 0.2-0.4 mg/100 mL to a concentration approaching that in adults. The α-tocopherol content of colostrum is about three times that of mature milk (mean values of 10 *vs.* 3 mg/L) (15). The ratio of α-tocopherol equivalents to PUFA (mg/g) declines from about 4.2 in colostrum to 0.6 in mature milk. In infants fed unmodified cow's milk, the plasma vitamin E level rises slowly, if at all, over a period of months. This difference in response is attributable to the much lower α-tocopherol content of cow's milk (0.1-0.8 mg/750 mL) (16). Formulae for infants based on cow's milk therefore were inadequate in vitamin E, particularly those that contained added PUFA and iron (17).

The rapid rise in plasma vitamin E in the nursing neonate indicates that the 2.0-2.5 mg of α-tocopherol per day provided by 750 mL of breast milk is adequate. The recommended intake of 3 mg/day allows for the increased requirement associated with the use of formulas containing added PUFA and iron.

The recommendations for children beyond infancy take into consideration the increasing intake of PUFA by growing children and the

sex difference in the PUFA intake of adults. The recommendations provide for a relatively uniform ratio of α-tocopherol equivalents to PUFA in the diet and are apparently adequate according to epidemiological data. They apply to mixed diets as consumed in Canada, including those that contain unusually high amounts of PUFA. The increased intake of PUFA in such diets is normally compensated for by an accompanying high amount of vitamin E. The increased vitamin E requirement associated with a high intake of PUFA does not necessarily result in an increased risk of vitamin E deficiency. Also, the protracted time required for concentrations of vitamin E in tissues to equilibrate with those in the plasma dampens the effect of short-term fluctuations in the intake of the vitamin (5).

Mixed diets as consumed by adults in Canada and the United States have been reported to provide 7-9 mg of *d*-α-tocopherol per day (2, 5, 18). If allowance is made for other vitamers, the *d*-α-tocopherol equivalents range from 8 to 11 mg/day. The recommended intakes of 6-10 mg of *d*-α-tocopherol equivalents per day therefore can be obtained from normal diets, and the general lack of deficiency signs in the population indicates that such diets meet the requirements of healthy adults. The recommended amounts will be exceeded by individuals who consume diets unusually high in PUFA. A compendium of vitamin E compounds in foods has been compiled by Bauernfeind (16). Hydrogenation increases the ratio of vitamin E to PUFA in vegetable oils.

There is no satisfactory evidence that the diets of Canadians are improved by supplements of vitamin E except in the case of infants fed formulae containing added PUFA and of individuals with malabsorption syndromes. Although supplements of vitamin E have been promoted for the aged, a recent study on animals has provided no evidence that the vitamin E requirement is increased during aging (18).

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Vitamin K

Vitamin K is the term for a group of natural and synthetic compounds that are derivatives of 2-methyl-1,4-naphthoquinone (mena-

dione, menaquinone-o). Phylloquinone (phytomenadione, vitamin K_1) occurs in plants. Various menaquinones (menaquinones-n, vitamin K_2), which differ in the length of their side chain, are found in animal tissues and in bacteria, including those of the intestinal tract (1, 2). Natural forms of vitamin K can therefore be obtained from both dietary sources and the products of bacterial metabolism in the intestine.

Vitamin K is required for clotting of the blood, and when there is a deficiency of it, the clotting time is prolonged, haemorrhages occur in the tissues and there may be internal and external bleeding (1, 3). Among the various factors that are involved in the process of coagulation are four vitamin K dependent proteins: prothrombin, proconvertin, the plasma thromboplastin Christmas factor and the Stuart-Prower factor (factors II, VII, IX and X, respectively). Vitamin K functions as a cofactor for the enzyme that carboxylates glutamyl residues of the precursor proteins to γ-carboxyglutamyl residues in the completed coagulation proteins (2). Other vitamin K dependent proteins containing γ-carboxyglutamyl residues have been found in various tissues, including bone (2).

Absorption of vitamin K from the intestine requires bile and pancreatic juice (1). A small reserve of the vitamin is stored in the liver (4). The principal forms in human liver, phylloquinone and menaquinone-7, indicate that both diet and intestinal bacteria are sources.

The amount of vitamin K in some foods has been determined by bioassay with chicks (1). Green leafy vegetables and liver are good sources of the vitamin. There are smaller amounts in meats and dairy products and low amounts in fruits and cereals (1).

The human requirement for vitamin K from dietary sources is not known. It has been suggested that as much as one-half of the body's need for it may be met by bacterial synthesis in the intestine (1).

The greatest need for vitamin K is during the time immediately after birth. The vitamin K status of the newborn is low since there is limited transfer of the vitamin across the placenta to the fetus, and the intestinal flora is not yet established (1). Levels of the coagulation factors dependent upon vitamin K decrease during the first few days after birth (1, 5, 6). Parenteral administration of 0.5-1.0 mg of vitamin K_1 to neonates has been recommended as prophylaxis against haemorrhagic disease of the newborn caused by a deficiency of the vitamin K dependent clotting factors (5, 6). This prophylactic measure is considered especially important for pre-term infants and for those of low birth weight, those who have had difficult births, those on antibiotics and those who are fed exclusively from the breast (5, 7). It has been recommended that formulae for infant feeding contain at least 4 μg of vitamin K, as phylloquinone, per 100 kcal (9.6 μg/1000 kJ) (6, 8). It is

usually necessary to add it to preparations not based on cow's milk.

With the exception of the newborn, a dietary deficiency of vitamin K is unlikely to occur in humans except under complicating conditions such as fat malabsorption or antibiotic therapy (3). In tests with vitamin K given intravenously to elderly individuals on antibiotic therapy, 0.03 μg of phylloquinone per kilogram of body weight was the minimum amount necessary to maintain clotting factors above base-line levels for 24 h, and 1.5 μg/kg was the minimum amount to achieve normal prothrombin time (9). These findings suggest that the requirement for the vitamin may lie somewhere between 0.03 and 1.5 μg of vitamin K_1 per kilogram of body weight per day.

The extent to which the requirement for vitamin K can be met by bacterial synthesis in the intestine is not known, and information on the amounts in foods is limited (1). At present there is insufficient information on which to base a recommendation for dietary intake of the vitamin.

Supplements of vitamin K are usually prescribed in medical therapy for conditions characterized by defective absorption of lipids, liver damage or changes in the intestinal flora induced by drugs (10), and it is often given to infants with chronic diarrhea (11).

Large doses of water soluble derivatives of menadione may be toxic. When formerly used in the treatment of the newborn, they were associated with hyperbilirubinaemia and kernicterus. Synthetic preparations of vitamin K_1 are now available for oral and parenteral use (5, 12). These should be used in routine prophylaxis for the newborn and they may also be the preferred forms for some therapeutic uses.

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VII. WATER-SOLUBLE VITAMINS

Vitamin C

Man is one of the relatively few species that are incapable of synthesizing ascorbic acid and thus are dependent on a dietary source of this vitamin. Dietary deprivation of it eventually gives rise to scurvy, a disease characterized by defective formation of collagen (1).

A precise biochemical function for ascorbic acid has not been elucidated. The only role in which it has been established as being essential is the hydroxylation of proline and lysine in the formation of collagen in connective tissue, osteoid tissue and dentin (2, 3). Other functions, listed below, have been suggested, although it is still not clear whether ascorbic acid is essential for these processes or serves only as a facilitator. These are metabolism of tyrosine (4), hydroxylation of tryptophan to 5-hydroxytryptophan (5) and dopamine to norepinephrine (6), microsomal drug metabolism (7) folic acid metabolism (8), iron absorption (9, 10) and transfer to ferritin (11). There is also some evidence for a role of ascorbic acid in the synthesis of carnitine (12), the conversion of cholesterol to bile acids (13), leukocyte function (14, 15) and the immune response (15), the blocking of nitrosamine formation in the gut (16, 17) and the detoxification of histamine in a number of stress situations (18, 19).

The Estimation of Requirements

Since an explicit metabolic function of ascorbic acid has not been established, a direct biochemical measurement of vitamin C status has not been developed. The estimation of human requirements for the vitamin has been made by indirect means from the amounts observed either to prevent or cure scurvy or to produce adequate reserves in tissues. More recently, the results of studies with radioisotopes have allowed calculation of the amount metabolized daily by the body.

An intake of 10 mg/day was established in a study at the Sorby Research Institute in Sheffield in 1944-1946 (20) and more recently

confirmed by Hodges *et al.* (21) as sufficient to cure clinical scurvy or to prevent signs of scurvy for an extended period (20). This level of intake, however, does not allow for adequate reserves in the body and may not completely fulfill all possible functions of this vitamin. Tissue reserves have been assessed mainly by concentrations in whole blood, plasma or leukocytes and by the appearance of significant amounts in urine.

At the onset of scurvy, with dietary intakes below 5 mg/day, levels of ascorbate in serum are 0.13 — 0.24 mg/100 mL (22), whereas the maximum serum level that can be attained, 1.0 — 1.4 mg/100 mL (23), requires intakes reported to range from 60 to 130 mg/day (23). An intermediate value of approximately 0.7 mg/100 mL may be reached with intakes of 50-75 mg/day (22-24) and an intake of 30 mg/day results in a serum level of approximately 0.5 mg/100 mL or less (24, 25).

At maximum levels of serum ascorbate, renal clearance of the vitamin increases sharply, which is taken to indicate saturation of the tissues. The results from excretion of excess ascorbic acid after a test load, which is indicative of saturation, led to recommendations of 25 to 160 mg/day (23). The necessity of maintaining the body in a state of saturation with ascorbic acid, however, is questionable.

Leukocytes become saturated when the intake is 75 mg/day (23, 24) although the results of one study have suggested that intakes of 12-22 mg/day will maintain saturation of the leukocytes for as long as 90 days in some people (26). Half saturation can be achieved on intakes of 45 mg/day (23, 24). Thus this approach has resulted in a wide variation in recommended intakes (23).

The results of experiments with ^{14}C- and ^{3}H-labelled ascorbic acid have provided estimates of the sizes of body pools and rates of turnover of vitamin C, the latter presumably indicating metabolic utilization and hence requirement.

The total body pool in healthy male adults is more than 1500 mg. An intake of about 200 mg/day has been shown to provide a pool of 2300-2800 mg (27) and a lower constant intake of 77.5 mg/day for 13 days, 1486-1542 mg (22, 28). Kallner *et al.* (29) observed pool sizes of 1500 and 1850 mg with intakes of 60 and 180 mg/day, respectively, in three subjects. Subsequently they obtained pools varying from 11 to 22 mg/kg of body weight in subjects who received amounts varying from 30 to 180 mg/day, which correspond to plasma levels ranging from 0.2 to 1.2 mg/100 mL (25).

During experimental depletion of ascorbic acid, signs of scurvy have appeared as the pool size fell below 300 mg (22, 28, 30) although psychological disturbances were apparent when it fell below 600 mg (31). Baker *et al.* (28, 30) found that restoration of the pool to 1500 mg was necessary before unchanged ascorbic acid began to appear in the

urine to indicate saturation of the tissues. Kallner *et al.* (25), however, observed that in non-depleted subjects there was a small but measurable excretion of ascorbic acid at intakes of 30 mg/day even though the pool was much smaller, about 800 mg (25, 29).

From the measurement of urinary radioactivity following the oral administration of [^{14}C] ascorbic acid to three hospitalized men without acute symptoms, Hellman and Burns (32) estimated total turnover rates of 0.66, 1.0 and 1.4 mg of ascorbic acid per kilogram of body weight per day (totals of 50, 59 and 90 mg/day). These values included any unchanged ascorbic acid as well as metabolites and thus presumably gave an overestimate of the amount actually metabolized.

Baker *et al.* (28, 30) found that excretion rates of metabolites of [^{14}C] ascorbate by adult male subjects who had been given an oral dose of it and then had the vitamin withdrawn from the diet ranged from 2.2 to 4.1 mg/day (mean, 2.9). Since the initial body pool was estimated to be approximately 1500 mg (28), the calculated turnover rate was 33.0 — 61.5 mg/day (mean, 45.0). This rate of catabolism remained relatively unchanged during a subsequent repletion period when the dietary intakes were up to 66.5 mg/day (28).

Kallner *et al.* (25) have more recently examined pool sizes and turnover rates in healthy male non-smoking adult subjects under steady state conditions of plasma ascorbate concentration. These subjects were maintained on supplements of 30, 60, 90 and 180 mg/day until a constant level in the plasma was attained, then were given a tracer dose of [^{14}C] ascorbate. Measurements of radioactivity in plasma and urine by pharmacokinetic principles suggested the existence of three pools: a central pool into which ascorbic acid is absorbed and from which it is excreted unchanged via the kidneys (representing renal turnover); a fast exchanging peripheral pool from which ascorbate metabolites are excreted (metabolic turnover); a deep slowly exchanging or storage pool. Total turnover and renal turnover were calculated from the total radioactivity and that associated with unchanged ascorbic acid, respectively, that appeared in the urine. The difference represented metabolic turnover. Total turnover was considered by the authors to reflect fairly accurately the amount of the dietary vitamin actually absorbed and was used instead of the intake as the basis for comparison with other measurements, since the turnover can be calculated from measured amounts. The dietary intake, although restricted, was somewhat variable. The metabolic turnover and hence the total turnover increased initially with increasing size of the supplement but gradually reached a maximum rate of 40-50 mg/day. At that level the total turnover was 60 mg/day and the renal turnover had become significant. These values also coincided with a plasma ascorbate level of 0.8 — 0.9 mg/100 mL and a total pool size approaching 20

mg/kg of body weight. On the premise that the rate of excretion of metabolites is a direct reflection of functional utilization, the authors suggested that a metabolic turnover of 40-50 mg/day is an appropriate goal, but to achieve this a total turnover of 60 mg is necessary, and when incomplete absorption (80-90%) is taken into account (33), a dietary intake of 70-75 mg/day is required. Further correction to allow for individual variation by the addition of 2 standard deviations (SD) to cover 95% of the population results in a recommended intake of 100 mg/day (1 SD from the calculations of the authors is 14 mg).

Several factors influence the blood levels and metabolism of ascorbic acid in varying degree although to what extent they alter requirements is debatable. There is some evidence that undue emotional stress in a normal person increases the rate of metabolism of ascorbic acid (30) although a higher requirement by patients with chronic mental disease has not been established (23). Equally equivocal is evidence suggesting higher requirements in people subjected to unusually low or high environmental temperatures or to excessive physical exertion (23). Women tend to have higher levels of ascorbate in plasma and leukocytes than men (34), which may be related to ovarian function since ascorbate levels fluctuate during the menstrual cycle (35). Oral contraceptives also tend to lower the concentrations of ascorbate in the plasma and leukocytes of women who use them (35, 36), but supplements of the vitamin do not necessarily improve their vitamin C status (37). On the other hand, sex differences in blood ascorbic acid levels persist into old age when the ovarian influence is no longer present (38).

Blood ascorbate levels tend to decrease gradually with age in adults (23, 39-41) although clinical scurvy is absent at levels usually associated with clinical symptoms in younger people (38, 39; 41). The levels rise rapidly when supplements are taken (42, 43) but fall with striking rapidity when they are withdrawn (39, 43). The significance of these observations in terms of requirements is difficult to assess. Very low blood ascorbate levels are more likely due to poor dietary intake of the vitamin than to the aging process (43, 44) but acute or chronic illness may further deplete body stores (45). There is at present insufficient evidence to define precisely the differences in requirements for ascorbic acid that are dependent on increasing age or on sex in the adult.

Cigarette smokers show markedly reduced plasma and leukocyte levels of ascorbic acid (40, 46, 47) that cannot be attributed to lower intakes (47). In the Canadian population, the smoking of less than 20 cigarettes per day is associated with a 25% lower plasma ascorbate level than that characteristic of non-smokers, and 20 or more per day are associated with a 40% reduction. On the basis of saturation studies,

Pelletier (47) has suggested that the major factor responsible for this is diminished intestinal absorption rather than enhanced metabolism. He estimates that smokers require twice as much ascorbic acid as non-smokers to maintain similar blood levels (48). On the other hand, using the same pharmacokinetic approach as with non-smokers (25), Kallner *et al.* (49) have demonstrated a marginal reduction in the absorption of ascorbic acid (76 *vs.* 84% in smokers and non-smokers respectively), a significantly higher rate of metabolic and total turnover and a shorter half-life of ascorbic acid (at low plasma concentrations) in male subjects who smoke more than 20 cigarettes per day as compared with non-smokers. The maximum metabolic turnover occurred in smokers on intakes of 70-90 mg/day, equivalent to a total turnover of 90 mg/day, whereas the plateau point for non-smokers was at intakes of 40-50 mg/day. Correcting for incomplete absorption and individual variation, these authors estimated the requirement for smokers to be in the region of 140 mg/day, which represents a 40% increase over the intake that they recommended for non-smokers (49).

Recommended Intakes

Adults

An intake of 30 mg of ascorbic acid per day (50) gives adequate protection against scurvy and provides for plasma ascorbate levels of about 0.5 mg/100 mL, as indicated by the results of studies with controlled intakes (24, 25). Information obtained from the national survey Nutrition Canada (51) showed that estimated intakes of 0-30 mg/day were associated with median plasma levels of 0.49-0.54 mg/100 mL for adult male non-smokers and 0.52 — 0.72 for female non-smokers (47). These levels fall within the low risk category of > 0.4 mg/100 mL set by the survey. An intake of 30 mg/day does not provide for full saturation of plasma or leukocytes with ascorbic acid (23). The levels in plasma and leukocytes that are considered to be consistent with good health, however, are presumptive quantities rather than those based on specific evidence, *i.e.*, it is assumed that full saturation is desirable although not essential and that something approaching half saturation is adequate. Excess above that required to saturate the blood is largely excreted in the urine and thus essentially wasted. In the absence of any other type of data, this assumption is reasonable.

Studies with radioisotopes have provided information on the rate at which ascorbic acid is metabolized and excreted via the kidneys and have given a more accurate measurement of the requirement. This approach, however, requires a number of theoretical assumptions, and so interpretation of the findings must be made with caution.

Information provided by these studies suggests a requirement considerably higher than 30 mg/day. Baker *et al.* (28, 30) interpreted

their findings to indicate a mean excretion rate of ascorbic acid metabolites of 45 mg/day. This figure has been questioned by Kallner *et al.* (25), who think that it may underestimate the metabolic rate in normal people since the study was made on subjects depleted of ascorbic acid, which would thus be drawn from the slowly exchanging deep storage pool, the faster exchanging central and peripheral pools having been exhausted early in the period of depletion. This may not be an entirely valid criticism since Baker *et al.* (28) noted little change in the rate of metabolism during the subsequent repletion period. Since the subjects in the studies by Baker *et al.* were smokers (52), the rate of metabolism of the vitamin may, in fact, be an overestimate of the rate in non-smokers. If the subjects were, on average, moderate smokers (< 20 cigarettes per day), the metabolic turnover of ascorbic acid might be anticipated to be 20-25% higher than in non-smokers, and thus an extrapolated metabolic turnover for non-smokers would be approximately 35 mg/day.

A maximum metabolic turnover rate of 40-50 mg of ascorbic acid per day, suggested by Kallner *et al.* (25), may, on the other hand, overestimate the requirement. Even though plasma levels had stabilized by the end of the equilibration period of 3 weeks, the shorter half-life of ascorbic acid at the higher total turnover rates suggested that full equilibration of dietary ascorbate with all pools had not occurred. Other information from the studies by Baker *et al.* (30) implies that at higher intakes only a limited amount of the ingested vitamin is equilibrated with the body pool. Ginter (53) has also suggested that some ascorbate pools in the body may exchange too slowly to achieve a steady state within a period of 3 weeks.

The significance of the dependency of the metabolic turnover on dietary intake or total turnover, as stated by Kallner *et al.* (25), is difficult to assess. These authors imply that the metabolic products excreted in the urine represent only the functional metabolism of the vitamin, thus as the intake increases, more is available to fulfil those metabolic functions, and when all of them are operating maximally, the rate of utilization of ascorbic acid and the production of metabolites necessarily plateau. The data do not preclude the possibility that an intake of 20-30 mg/day is adequate to saturate all systems and that metabolism of excess vitamin occurs with increasing intake until a maximum capacity of the tissues is reached. This seems a less likely explanation since the renal threshold already presents a very efficient mechanism of ridding the body of excess ascorbic acid that comes into play well before the plasma is saturated. It seems unnecessary to postulate another mechanism that becomes active at moderate levels of ascorbate in tissue and plasma. Further, it is now well established that there is no appreciable degradation of ascorbic acid to carbon dioxide

in man (30), and if sulphated or methylated derivatives, which are considered to be general products of degradation, are present in urine, they are in very small quantities. Except for oxalic acid, the major urinary metabolites in man have not yet been identified (54).

When all of the available information is considered, that obtained from the studies with radioactive isotopes would seem to provide a more solid and better basis for establishing a requirement for ascorbic acid than approaches used previously. Until further research can resolve the discrepancy between the two reported turnover rates discussed above, however, a rational approach would be to assume a metabolic turnover of ascorbic acid midway between 35 and 45 mg/day, *i.e.*, a total of 40 mg/day, to be a reasonable estimate of requirement. Correction for incomplete (85%) absorption (33) gives a value of 46 mg/day. Because of the design of their study, Kallner *et al.* (25) could not calculate the variance of the total turnover rate on the basis of intra-individual variation. For the purpose of the present dietary recommendation, a coefficient of variance of 15%, which is characteristic of much quantitative biology, was used to adjust for population variance. Thus a correction factor of 30% (2 SD) gives a recommended intake of 60 mg/day for the adult non-smoking male.

In view of the most recent evidence for the effect of smoking on the metabolic turnover of ascorbic acid (49) and the well-documented low levels of blood ascorbate in smokers, it would seem justifiable to advise people who smoke 20 or more cigarettes per day to increase their intake of ascorbic acid by about 40%, *i.e.*, to 80-85 mg/day. This level of increase is in line with that suggested by Kallner *et al.* (49) but it is intended to serve only as a rough guide until more and confirmatory information on the subject is available.

Results of studies on turnover as an index of requirement for vitamin C are accepted, but it is noted that at present there is no documented quantitative relationship between this measure and expressions of functional performance. That is, a precise linkage to some level of health remains undefined. This is a serious limitation to the present use of the results of studies on metabolic turnover as criteria of a nutrient requirement, but in this case no other satisfactory criteria are available. Although intakes sufficient to prevent scurvy (about 10 mg/day) can be defined, these would be inappropriate as the basis of a recommended intake. It is hoped that with further research a more precisely defined basis for the estimation of requirements for vitamin C will be found.

To date, published studies on turnover have dealt with young adult male subjects only. It is judged that the most appropriate approach to extension of the findings to females and to other age groups is to assume that the size of the body pool and hence the requirement

for ascorbic acid is related to body size in a manner analogous to the relationship between body size and basal metabolic rate (BMR). On that basis, the recommended intake for the adult male (19+ years of age) is 60 mg/day and for the adult female, 45 mg/day. No adjustment is proposed for weight differences within these categories and none is suggested for increasing age although it is recognized that the BMR decreases with age.

Pregnancy

The plasma level of ascorbic acid falls progressively during pregnancy (55-57) although the decline is more obvious when intakes are moderate (<80 mg/day) or low (<40 mg/day) (55). There appears to be a placental transfer of ascorbic acid to the fetus from the mother such that cord and fetal plasma levels are 50% above maternal levels (58). An additional 20 mg/day of ascorbic acid is recommended for the last two trimesters of pregnancy.

Lactation

The ascorbic acid content of human breast milk varies with the dietary intake (59-61). Most reported values fall within a range of 3-5 mg/100 mL (59-62); therefore the secretion of 750 mL of milk per day would result in a corresponding loss of 23-38 mg of ascorbic acid. The additional ascorbic acid recommended during lactation is 30 mg/day.

Infants, Children and Adolescents

Newborn infants, especially if premature, may have an increased need for vitamin C during the first days of life to prevent neonatal tyrosinaemia and tyrosinuria (63, 64). It is not known whether or not transient neonatal tyrosinaemia is harmless, but as a safety measure, it has been suggested that a supplement of about 100 mg of ascorbic acid be provided during the first week. This should not be considered as a recommended intake in the sense that this term is used elsewhere in this document.

There is little precise information on requirements for ascorbic acid in infancy and childhood. Infants fed at the breast, with intakes of 7-17 mg/day (65), and those fed otherwise, with an intake of 7 mg/day (66), are protected from scurvy. Since the ascorbic acid content of breast milk ranges from 3 to 5 mg/100 mL (59-61), a daily consumption of about 750 mL would provide 23-38 mg. Thus an intake of at least 20 mg/day should provide an adequate margin for the first 6 months of life to support requirements for maintenance and growth and to allow for the establishment of generous stores. Theoretical accretion rates for ascorbic acid during infancy and childhood are less than 1 mg/day.

In the absence of specific data concerning the requirements of

succeeding age groups for vitamin C, a reasonable approach is to assume that they are related to body size in a manner analogous to the relation between body size and BMR. As for adults, therefore, estimates of requirements for various age and sex groups up to adulthood have been based upon mean BMRs, but it is thought to be inappropriate to make this adjustment when it would bring the recommended intake below 20 mg/day. Adjustment to BMR is therefore used for children after the age of 4. Below that age 20 mg/day are recommended.

Comment on Very Large Intakes

Intakes of ascorbic acid in gram quantities per day have been proposed as a therapeutic measure in the treatment of colds and various infections (67), cancer (68), mental illness (69), hypercholesterolaemia and atherosclerosis (70) etc., but at the present time there is little substantiation for these claims (71). Although ascorbic acid is considered in general to be non-toxic, when it is taken in such large doses it may have untoward effects (71). Long-term intakes of large amounts are not recommended without medical supervision. The absorption of ascorbic acid is less efficient as intakes rise above 180 mg/day, falling from 80-90% to 50% at 1.5 g/day (72, 73) and to as low as 16% at intakes of 12 g/day (72).

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Thiamin

Thiamin, as the pyrophosphate, is a coenzyme in the oxidative decarboxylation of α-keto acids such as pyruvic and α-ketoglutaric (1). Thiamin pyrophosphate is also a coenzyme for transketolase, the enzyme that catalyzes the interconversion of sugars that contain 3, 4, 5, 6 or 7 carbon atoms per molecule. The oxidative decarboxylation of pyruvate and α-ketoglutarate is important in the physiological production of energy, and the requirement for thiamin is thus related to energy expenditure. There is some indication that dietary fat to some extent spares thiamin (2,3). Most studies on thiamin requirements, however, have been done with subjects on diets similar to those commonly consumed in Canada, in which variation in the ratio of fat to carbohydrate is small in comparison with the ratio that might affect the requirement for thiamin. In general, the intake of thiamin need not be adjusted for the relative amounts of dietary carbohydrate and fat.

Beriberi is the classical pathological condition associated with a deficiency of thiamin (1,4). In western countries, deficiency most often is associated with alcoholism. During starvation or semi-starvation, tissue stores of thiamin are rapidly depleted (5).

Requirements and Recommended Intakes

Adults

The requirement for thiamin has been found to be proportional to the intake of energy when the dietary energy is varied by adjusting the intake of carbohydrate (6); but it is really related to the utilization of energy, so there is still a requirement even when no food is eaten. Sauberlich *et al.* (6) found the average requirement for thiamin to be 0.30 mg/1000 kcal (0.36 mg/5000 kJ) on the basis of urinary excretion of the vitamin and transketolase activity in erythrocytes. Others have suggested that the average requirement is approximately 0.33 mg/1000 kcal (0.39 mg/5000 kJ) (7,8). On the basis of their findings, Daum *et al.* (9) proposed 0.63 mg/day or 0.25-0.30 mg/1000 kcal (0.30-0.36 mg/5000 kJ) as the average range of requirement for healthy young women. Elsom *et al.* (10) also found intakes of 0.60-0.70 mg/day (0.35 mg/1000 kcal (0.42 mg/5000 kJ) to be adequate for women. Intakes of 0.18-0.22 mg/1000 kcal (0.22-0.26 mg/5000 kJ) by adults have been reported to result in clinical signs indicative of deficiency (11-13).

On the basis of these findings, the average requirement for thiamin to prevent signs of depletion is taken to be 0.30 mg/1000 kcal (0.36 mg/5000 kJ), which, on the assumption that the coefficient of variation is 15%, supports a recommended intake of 0.40 mg/1000 kcal (0.48 mg/5000 kJ) (representing a mean + 2 SD). The requirement of older adults may be higher than that of young adults (14) but there are

insufficient data upon which to base a different recommendation. There is also no clear evidence that there is a corresponding decrease in the requirement for thiamin when the intake of energy falls to levels of 1800-2000 kcal/day (7600-8400 kJ/day) and below. It is known that a decrease in the intake of food, as in weight reduction programs, does not correspondingly affect the need for thiamin because of its relation to energy expenditure. It is therefore recommended that the intake should not be lower than 0.80 mg/day by people 19 years of age and older regardless of the energy intake.

Infants

Because information on the thiamin needs of infants is so limited and because there is no indication that they are different from those of older age groups, an intake of 0.40 mg/1000 kcal (0.48 mg/5000 kJ) is recommended. It is recognized that this may be higher than the level secreted in breast milk by well-nourished mothers but likewise there is no evidence that the levels in breast milk are not adequate. The recommended amount should be applied in the formulation of substitutes for breast milk and in the complementary feeding of older infants.

Children and Adolescents

There have been very few studies on the requirements of children and adolescents for thiamin. The results of studies with children from pre-school age to 13 years have suggested that intakes of 0.70-1.40 mg/day (15) and of 0.45-0.50 mg/1000 kcal (0.54-0.60 mg/5000 kJ) (16,17) are adequate. On the other hand, average intakes of 0.30 mg/1000 kcal (0.36 mg/5000 kJ) for adolescent girls (18) and of 0.28 mg/1000 kcal (0.33 mg/5000 kJ) for adolescent boys (19) have been considered marginal or inadequate although an intake of 0.38 mg/1000 kcal (0.45 mg/5000 kJ) was considered adequate for boys (19). Boyden and Erikson (20), however, found that an average intake of 0.32 mg/1000 kcal (0.38 mg/5000 kJ) was adequate for pre-adolescent children. Based on these limited data, the recommended amount for adults, 0.40 mg/1000 kcal (0.48 mg/5000 kJ), seems appropriate for children and adolescents.

Pregnancy

Studies on the thiamin status of pregnant women have indicated that the requirement is increased during pregnancy (21,22). Oldham *et al.* (23), however, did not find evidence for an increased need during pregnancy, and Heller *et al.* (21) found no correlation between thiamin status and the course and outcome of pregnancy. It is questionable, therefore, that a special recommendation should be made for pregnancy except for the increased amount needed for the metabolism of the extra energy that is required. The recommendation therefore remains at 0.40 mg/1000 kcal (0.48 mg/5000 kJ).

Lactation

The thiamin content of human milk has been found to vary appreciably with a mean of approximately 16 μg/100 mL (24-26). If a lactating woman secretes 750 mL of milk per day, the output of thiamin is approximately 0.1 mg/day. If 450 kcal (1900 kJ) of food energy per day with the recommended amount of thiamin at 0.40 mg/1000 kcal (0.48 mg/5000 kJ) are added, an additional amount of 0.18 mg of thiamin per day should be adequate.

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Riboflavin

Riboflavin is a constituent of the coenzymes flavin adenine dinucleotide and riboflavin 5′-phosphate (1). The flavoproteins function as enzymes in tissue respiration and in the direct oxidation of substrates by oxygen.

Requirements and Recommended Intakes

Recommended dietary intakes of riboflavin have been related to the intakes of energy (2, 3) and of protein (1, 4) and to metabolic body size (5). The method of expression has little influence on estimated requirements for riboflavin as averages for groups because of the interdependence of metabolic body size and requirements for energy and protein. Various methods produce different estimates at extremes of body weights within an age-sex group, which imply different effects of physical activity (and associated energy requirement) upon the requirement for riboflavin. For practical reasons, recommended intakes are expressed in relation to energy utilized, but caution should be used in applying them at extremes of body weight and to unusual levels of physical activity.

A deficiency of riboflavin in man is characterized by a variety of symptoms including soreness of the tongue and lips and seborrhoeic dermatitis (1).

Adults

Clinical symptoms of riboflavin deficiency have been recorded for adults on diets containing 0.25 mg/1000 kcal (0.30 mg/5000 kJ) or less (6) but intakes of 0.28-0.35 mg/1000 kcal (0.34-0.42 mg/5000 kJ) have not produced signs of deficiency (7-10). It has been shown that the urinary excretion of riboflavin increases sharply when intakes are above 0.50 mg/1000 kcal (0.60 mg/5000 kJ) (7, 9, 11, 12), and glutathione reductase activity in erythrocytes increases sharply in response to the addition of flavin adenine dinucleotide *in vitro* when intakes have been lower than that (13).

These findings suggest that an intake of 0.50 mg/1000 kcal (0.60 mg/5000 kJ) is adequate to meet the needs of almost all people, and it is adopted as the recommended intake for adults, for whom the intake should not fall below 1 mg/day. If the coefficient of variation is about 15%, the average requirement is somewhat below 0.40 mg/1000 kcal (0.48 mg/5000 kJ) but it is not possible to estimate precisely an average requirement from the available data.

Several investigators have suggested that oral contraceptives may increase the requirement for riboflavin (14) but there is insufficient knowledge to justify recommendation of a higher intake.

Infants, Children and Adolescents

Very little information is available on the riboflavin requirements of infants and children. Snyderman *et al.* (15) found that an intake of 0.40 mg/day (approximately 0.45 mg/1000 kcal (0.54 mg/5000 kJ)) restored and maintained riboflavin equilibrium in infants weighing 8-9 kg. Oldham *et al.* (16) found that the urinary excretion of riboflavin by children increased above a baseline level at intakes of about 0.50 mg/1000 kcal (0.60 mg/5000 kJ). The recommended intake is the same as for adults, namely 0.50 mg/1000 kcal (0.60 mg/5000 kJ).

Pregnancy

Findings by Oldham *et al.* (17) suggested that an intake of at least 0.9 mg of riboflavin per day is required during pregnancy but Brzezinski *et al.* (18) reported some signs of clinical deficiency among pregnant women on intakes of 0.7-1.3 mg/day and also evidence of an increased requirement as pregnancy progresses. Heller *et al.* (19) also found evidence for an increased requirement for riboflavin during pregnancy but found no correlation between signs of deficiency and the outcome of pregnancy.

The suggested increase in energy requirement during pregnancy would imply an increase of about 0.15 mg of riboflavin per day, which may be inadequate to meet the needs implied by the findings noted above. The recommended intake during pregnancy is 0.30 mg/day above that for the non-pregnant woman.

Lactation

The riboflavin content of breast milk varies appreciably. Mean values generally fall between 25 and 35 μg/100 mL (20-22). An important factor in this variation is that the content is affected within a matter of hours by the amount in the food consumed (20, 21). If an average of 750 mL of milk is secreted per day with an average riboflavin content of 30 μg/100 mL and a 70% efficiency of its utilization for milk production (23), an additional 0.3 mg/day is needed to cover the loss. The suggested increase in energy requirement during lactation, 450 kcal/day (1900 kJ/day) would imply an increase in the need for riboflavin of 0.2 mg/day, which is below that needed for milk secretion. The recommended intake for lactating women is 0.4 mg/day above that for nonlactating women.

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Niacin

Niacin is the generic term for nicotinic acid and its derivatives that have the same biological activity (1). Nicotinamide (niacinamide) is the active form and functions in various metabolic processes, including tissue respiration, as part of the coenzymes nicotinamide adenine dinucleotide and its phosphate.

Estimation of requirements is complicated by the fact that the biological availability of preformed niacin from some foods, particularly cereals, is poor, and that some tryptophan is oxidized to niacin (2-4). It has been estimated that about 3% of ingested tryptophan is thus converted and that 60 mg provides 1 mg of niacin (2-4). Because of this relationship, the recommended intakes of niacin are expressed as niacin equivalents (NE), 1 NE being equal to 1 mg of niacin or 60 mg of tryptophan Data from the Nutrition Canada survey (5) indicate that the average Canadian diet provides approximately 13 NE/1000 kcal (16 NE/5000 kJ). The effective intake would be slightly lower if the biological availability of preformed niacin were taken into account.

A deficiency of niacin results in pellagra, which is characterized by dermatitis, inflammation of the mucous membranes and dementia (6).

Requirements and Recommended Intakes

Adults

The basic sources of information about human requirements for niacin are studies by Goldsmith *et al.* (7-11) and Horwitt *et al.* (2, 12, 13). Both groups agreed that an intake of about 9 NE/day prevents pellagra. This amount is equivalent to about 4.4 NE/1000 kcal (5.2 NE/5000 kJ) (13).

Although evidence that the requirement for niacin is related to the expenditure of energy rather than to a measure of body size is weak, it is a convenient mode of expression. An average intake of about 5.5 NE/1000 kcal (6.6 NE/5000 kJ) produces a clear increase in the urinary excretion of metabolites of niacin (2). If a factor of 30% is taken as appropriate to allow for individual variability of requirement, the recommended intake for adults on that basis is 7.2 NE/1000 kcal (8.6 NE/5000 kJ). This is based on energy utilized, so there is a requirement even during fasting. There is no information on what the requirement for niacin may be at low intakes of energy by adults, but as a safety factor it is recommended that the intake should not be lower than that based on 2000 kcal/day (8400 kJ/day), *i.e.*, 14.4 NE/day, by people 19 years of age and older.

Oral contraceptives appear to enhance the conversion of tryptophan to niacin (14) but there are insufficient data upon which to base any special recommendation for women who use them.

Infants, Children and Adolescents

There are no data on the niacin requirements of infants, children and adolescents. Since breast milk provides 6.2-7.6 NE/1000 kcal (7.4-9.8 NE/5000 kJ) (15-17), the recommended intake is the same as that for adults, and likewise for children and adolescents, namely 7.2 NE/1000 kcal (8.6 NE/5000 kJ).

Pregnancy

There is no information on the niacin requirement during pregnancy. Wertz *et al.* (18) have suggested that the conversion of tryptophan to niacin may be more efficient during pregnancy. Under these circumstances it is recommended that the intake during pregnancy be increased in proportion to the higher intake of energy that is recommended, *i.e.*, by about 2 NE/day. The extra protein that is recommended should contain more than enough tryptophan to supply an additional 2 NE/day.

Lactation

Human milk contains about 180-230 μg of preformed niacin and 19-21 mg of tryptophan per 100 mL (15-17). If 750 mL are secreted per

day, about 1.5 mg of preformed niacin and 2.5 NE as tryptophan are lost. The extra intake of energy that is recommended, 450 kcal/day (1900 kJ/day), would increase the requirement by about 3 NE/day. The additional dietary protein that is recommended would increase the intake of niacin equivalents as tryptophan. The recommended intake of niacin during lactation is the same as that for non-lactating women, 7.2 NE/1000 kcal (8.6 NE/5000 kJ).

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Vitamin B_6

The term vitamin B_6 refers to three related and metabolically interconvertible substances, pyridoxine, pyridoxal and pyridoxamine, and their derivatives (1). The biochemically active form, pyridoxal 5-phosphate, is a coenzyme in numerous metabolic reactions involving amino acids (2), carbohydrates (3) and unsaturated fatty acids (4). These metabolic functions have been the subject of many reviews (2, 3, 5-7).

Vitamin B_6 is widely distributed in nature. Meat, fish, poultry, milk and whole grain cereals are good dietary sources (8).

Deficiency of vitamin B_6 produces a wide range of physiological and metabolic changes. Primary deficiency in man is rare, however, which suggests that usual intakes are above requirements. The usual approach to the estimation of requirements for vitamin B_6 involves the depletion of subjects followed by repletion with known amounts. Criteria of adequacy have usually been based on biochemical measurements although changes in electroencephalographic patterns have also been described in deficiency. The biochemical indices have included the following (9): the urinary excretion of vitamin B_6 and 4-pyridoxic acid, of taurine and of metabolites of tryptophan after a loading dose of that amino acid; plasma levels of pyridoxal phosphate; aspartate and alanine aminotransferases in serum or erythrocytes; plasma levels of amino acids.

Requirements and Recommended Intakes

Adults

Using such criteria, several investigators have reported that the amount of vitamin B_6 required to restore the nutritional status of deficient animals and human subjects to normal is directly related to the dietary intake of protein (10 16). The results of several studies suggest that a ratio of about 0.015 mg of pyridoxine per gram of dietary protein will normalize the excretion of tryptophan metabolites in almost all young adult subjects (10, 13, 15, 17-21), *i. e.*, that amount seems to include an allowance for individual variability. Accordingly, this ratio is accepted as the basis of the recommended intake of vitamin B_6 for the normal adult.

When the intake is expressed as milligrams per day it therefore varies with the intake of protein. For example, at the level of the recommended intake of protein, 57 and 41 g/day for adult men and women, respectively, the recommended amounts of vitamin B_6 are 0.9 and 0.6 mg/day; and at the level of the average intakes of protein reported in the Nutrition Canada survey (22) by young adult men and women, 120 and 70 g/day, respectively, the recommended amounts of vitamin B_6 are 1.8 and 1.1 mg/day. For people whose intakes of protein are in the upper portion of the range, the recommended intakes of vitamin B_6 might be about 30% higher. It must be emphasized, therefore, that in the present report the recommended intakes of this vitamin are expressed on this basis and that any expression in milligrams per day is derived from the relationship with the dietary protein.

There have been several reports in recent years that the use of anovulatory steroids alters many of the biochemical indices of nutritional status involving vitamin B_6 (18, 23-28), but the lower doses of those preparations that are now in general use may have less effect. Recent reports also suggest that the needs for vitamin B_6 of users of oral contraceptives appear to be close to those of non-users (29, 30). Thus, although daily supplementation with 50 mg of pyridoxine hydrochloride has been reported to alleviate depression in users of oral contraceptive steroids (31), the present state of knowledge does not justify a recommendation of extra vitamin B_6 for women who use them (19).

Infants

Clincial signs of vitamin B_6 deficiency have been reported in two breastfed infants whose mothers' milk supplied 0.05-0.06 mg/L (32). An intake of 0.015 mg/g of protein appears to be adequate to cover the needs of all normal infants who are fed formulae (33). This value is close to the 0.013 mg/g of protein reported to be present in the milk of

women whose intakes of vitamin B_6 are less than 2.5 mg/day. The recommended intake of this vitamin for infants is 0.015 mg/g of protein, the same as for adults.

Children and Adolescents

A satisfactory evaluation of the requirements of children and adolescents for vitamin B_6 is not possible on the basis of available data (33, 34). Reports on intakes suggest that a recommended amount of 0.015 mg/g of protein is appropriate also for these age groups (35-37).

Pregnancy

A pregnant woman must receive enough vitamin B_6 to supply the fetus with a sufficient quantity to support its metabolism of amino acids and to meet her own needs; and she must also supply a small quantity for accumulation in the fetal tissues. The placenta seems to concentrate vitamin B_6 since the concentration in cord blood is considerably higher than that in maternal blood (38-44).

As with users of oral contraceptives, abnormalities in biochemical indices of nutritional status in vitamin B_6, perhaps attributable to an increased production of oestrogens, have been reported in pregnant women (39-43, 45-49). Several workers have reported that these indices can be restored to values characteristic of nonpregnancy by the administration of vitamin B_6 (39, 42-45, 48). Although an increased requirement has been suggested on this basis, Hillman *et al.* (50) have questioned a need for supplementation with vitamin B_6 during pregnancy. There is no substantive evidence that pregnancy imposes any specific demands on the metabolism of vitamin B_6 but quantitatively there should be enough to supply the small amount deposited in the fetus. The recommended intake during pregnancy is 0.015 mg/g of dietary protein. If the intake of protein is increased, the intake of vitamin B_6 should be increased proportionately.

Lactation

The concentration of vitamin B_6 in breast milk ranges from 0.008-0.016 mg/L during the first few days of lactation to 0.08-0.18 mg/L in mature milk (44, 51-53). It varies with the intake (51). In the milk of women who ingest usual levels of the vitamin it is somewhat less than 0.015 mg/g of protein secreted.

As with pregnancy, there is no indication that lactation imposes a specific alteration in the metabolism of vitamin B_6, and any increase in requirement would be related to the process of milk secretion. The recommended intake for nonlactating women, 0.015 mg/g of dietary protein, would provide vitamin B_6 at somewhat greater levels than are secreted in milk. The demand for the vitamin associated with amino

acid metabolism in the formation of milk protein is not known. On the assumption that it is the same as that for other aspects of protein metabolism and that at full lactation the increase in protein utilization is about 20 g/day, the net increase in the requirement for vitamin B_6 would be about 0.3 mg/day. The recommended intake for lactation, therefore, is 0.015 mg/g of dietary protein plus an additional amount of 0.3 mg/day.

Excessive Intake

Vitamin B_6 appears to have very low toxicity (54) but a transient dependency has been induced in adults given 200 mg of pyridoxine hydrochloride per day for 33 days and then returned to normal dietary intakes (55).

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Folacin

Folacin (folate) is the term used to describe a group of coenzymes and their precursors that have a pteroylglutamate structure. Polyglutamate conjugates, in which various numbers of L-glutamate residues are linked by peptide bonds between α-amino groups and γ-carboxyl groups, occur in foods and tissues. There is considerable evidence that most of the folacin presented to the mammalian intestine enters the portal venous circulation as monoglutamate (1-5), with possibly a small proportion as di- or triglutamate. Monoglutamate can be transported as such (6), but reduced folates are probably methylated and enter the portal vein as methyltetrahydrofolate (7-9). The folate coenzymes function biochemically in purine synthesis, in the conversion of deoxyuridylate to thymidylate in DNA synthesis and in many other biochemical reactions. Most of the clinical manifestations of folacin deficiency are due to deficiency of 5,10-methylenetetrahydrofolate, a coenzyme and methyl donor in the conversion of deoxyuridylate to thymidylate (10).

Body Stores

The main storage organ for folacin is the liver. Analysis of autopsy specimens from people killed by accident in Canada showed a mean ± SD value of 7.8 ± 2.3 μg of folacin per gram of liver tissue (11). Red blood cells acquire their folacin during development and retain it during most of their life span. When dietary folacin is withheld, the level in the serum becomes subnormal within 2-3 weeks whereas that in the circulating red cells falls progressively over several months. In one healthy American on a diet almost free of folacin, the serum concentration became low in 2-3 weeks, the red cell concentration became low in 17-18 weeks and megaloblastic anaemia developed after 4 ½ months (12).

Folacin in Food

Folacin is present in many foods, including vegetables, fruits, dairy products, meat and liver (13, 14). It is present in a variety of

forms, as monoglutamate and polyglutamates ranging up to at least seven glutamate moieties. It is usually assayed microbiologically with *Lactobacillus casei*. When used directly, this method measures mono-, di- and triglutamates, often referred to as free folacin (15). The higher polyglutamates are measured by the same assay after conversion to simpler forms by the action of glutamyl carboxypeptidase (conjugase). After this treatment the folacin measured in biological material is called total folacin.

Some early attempts by Chanarin *et al.* (16) in assaying diets gave total values four or more times higher than those for free folacin, but the validity has since been questioned by some of the same authors (17) and the high values may well have been erroneous. It should also be noted that many foods have endogenous conjugases that may initiate the process of deconjugation unless special steps are taken to prevent their action (18). Since it is mainly the monoglutamate form that is absorbed from the intestine, this may be a biologically advantageous situation; but the activity of these enzymes may also be responsible for some of the findings that have resulted in confusion in reports on the relative proportions of free and total folacin in various diets.

Assays of foods prepared for eating have shown ratios of free to total folate in mixed diets of 1:1.2 (19) and 1:2 (20).

Adequacy of Canadian Diets

The national survey, Nutrition Canada (21), found that the mean daily intake of total folacin by males aged 12-64 was 205 μg and for females of the same ages 149 μg. That these intakes are adequate may be inferred from the results of analysis of autopsy specimens of liver, which indicated that Canadians have adequate liver stores of folacin (11). It was also found that the concentrations of folacin in liver samples from men and women are similar, which suggests that women require less to maintain adequate stores. This may be acknowledged by expressing requirement in terms of micrograms per kilogram of body weight.

Absorption

The mean absorption by normal subjects of a physiological amount of pteroylglutamic acid is about 85% (22-25), with a range of about 50-94%. Accordingly, the minimal daily requirement of pteroylglutamic acid must be multiplied by a factor of 100/85 to convert it to the amount that the average person must receive by mouth, and a factor of 2 must be used to accommodate the lowest absorption that has been observed (50%).

The literature on the absorbability of polyglutamate forms is inconclusive, some investigators finding that equimolar amounts of

mono- and polyglutamates are absorbed equally well and others that polyglutamate forms are less well absorbed (26). Halsted *et al.* (27, 28), in an intestinal perfusion study on nine volunteers, found that the absorption of heptaglutamate was an average of 70% of that of pteroylmonoglutamate. This factor may be used to correct for the absorbability of all polyglutamates, since absorbability decreases with increasing chain length. If, as now seems likely, dietary folacin is 50% free and 50% bound, the overall absorbability should be 85% of that of pteroylglutamic acid. The requirement for total folate therefore would be 1.2 times that of free folate.

Recommended Intakes

Adults

It has been found that most adults with anaemia resulting from folate deficiency respond haematologically to daily supplements of 100 μg of pteroylglutamic acid or less, but in most studies of such cases the contribution of the dietary folate was not measured. In one subject on a diet that provided no folacin a good response to the daily injection of 50 μg of pteroylglutamic acid was obtained (29).

The results of prophylactic studies that were made on small numbers of individuals by two groups of investigators have indicated that about 100 μg of pteroylglutamic acid per day will prevent the development of deficiency (30, 31).

From this figure of 100 μg, a recommended amount per day is estimated as follows. It is multiplied by 2 to accommodate for least possible efficiency of absorption and by 1.18 to correct for the less efficient utilization of polyglutamates from a mixed diet. The product is 236.

The average intakes of folacin by adult Canadians are 205 μg/day for men and 149 for women (21), and these amounts apparently permit the maintenance of adequate stores. From these considerations the recommended dietary intake of total folate is 3 μg/kg of body weight per day, which respectively becomes 210 and 165 μg/day for a man of 70 kg and a woman of 55 kg.

Pregnancy

The requirement for folacin is increased during pregnancy (26). Studies on the treatment of pregnant women with anaemia from folate deficiency have shown that relatively large amounts may be needed to produce a haematological response, but this may be because of preferential transfer of administered folate to the fetus. Prophylactic studies in which pregnant women received supplements of 100-200 μg of pteroylglutamic acid per day have indicated that a total intake of about 400 μg/day will provide homeostasis. On the basis of these findings, a dietary intake of 470 μg (*i.e.*, 400 × 1.18) per day, or 8 μg/kg of body

weight per day during pregnancy is recommended. Pharmaceutical supplements are more effectively utilized. There is epidemiological evidence that without significant increases in the intake of folacin (dietary or supplemental) many pregnant women develop signs of deficiency.

Lactation

Since lactating women secrete about 50 μg of folate per day in milk, the recommended intake during lactation is 120 μg/day above that for non-pregnant non-lactating women.

Infants and Children up to 4 Years of Age

Full-term infants fed from the breast receive about 50 μg of folacin per day and do not develop a deficiency. Studies in an orphanage population have shown that children receiving 5 μg/kg of body weight per day, mostly as pteroylglutamic acid, do not become deficient. It is therefore recommended that, in terms of total folate, the intake should be 50 μg/day or 6 μg/kg of body weight per day, whichever is more.

Children 4-13 Years of Age

There are no data available on requirements for this age group. Presumably, after the early growth spurt, the requirements approach those of adults. From 4 to 13 years of age, 5 μg/kg per day is considered adequate, and after that, the adult figure, 3 μg/kg per day can be taken as appropriate.

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Vitamin B_{12}

The B_{12} vitamins are characterized by a corrin ring with a cobalt atom in its centre to which are attached 5,6-dimethylbenzimidazole,

ribose and a methyl, deoxyadenosine, hydroxo or cyanide ligand.

A number of reactions dependent upon vitamin B_{12} occur in the intermediary metabolism of bacteria, but only two of these are known to occur in man, *viz.*, the conversion of N^5-methyltetrahydrofolate to tetrahydrofolate (1,2) and of methylmalonyl-CoA to succinyl-CoA (3). The vitamin is probably also involved in other biochemical reactions in man that have not been completely defined.

Sources

Vitamin B_{12} is produced almost exclusively by bacterial synthesis. It is required by all higher animals, which acquire tissue stores of it and in turn become the chief dietary sources of the vitamin for man. Plants grown under sterile conditions contain little or no vitamin B_{12} but those grown under natural conditions may contain small amounts, probably because of contamination by soil bacteria. Some bacteria in the human colon synthesize the vitamin but this is unavailable to the host. There are some in the human small intestine, however, that also synthesize it (4), and this fraction may be absorbed.

The average diet of North Americans provides 5-15 μg of vitamin B_{12} per day (5). The vitamin is relatively heat stable and losses in cooking are therefore not nearly as great as in the case of folic acid.

Metabolism and Deficiency

For normal absorption, vitamin B_{12} must combine with intrinsic factor, a glycoprotein secreted by the gastric parietal cells. The complex thus formed becomes attached to specific receptors on the ileal enterocyte (6). The vitamin enters the enterocyte and the intrinsic factor probably remains on the cell surface. The vitamin combines with the transport protein transcobalamin II, enters the portal circulation and is then distributed via the systemic circulation to all body tissues. The complex with transcobalamin II is taken up by the body cells. Subsequently some of the vitamin reenters the circulation bound to another protein, cobalophilin. This complex serves as a storage form of vitamin B_{12} and its analogues and as a means of transport to the liver for excretion in the bile. In normal subjects the vitamin B_{12} thus excreted is liberated from its complex with cobalophalin by the action of digestive enzymes, becomes bound to free intrinsic factor and is reabsorbed, thus establishing an enterohepatic cycle (7). The excreted analogues of the vitamin do not become bound to intrinsic factor and are mostly lost from the body.

The amount of vitamin B_{12} that can be absorbed at one time from the intestine is limited (8), probably because of saturation of the ileal receptors. Absorption from whole diets has not been extensively stud-

ied. Its absorption from liver and milk is similar to that from an aqueous solution (9) but it is not so well absorbed from eggs (10).

Serum Concentration

Measurement of the concentration of the vitamin in the serum (by microbiological or radioisotopic methods) provides an index of the state of vitamin B_{12} nutriture. Assays in different laboratories are not necessarily comparable, but values below 80 pg/mL are usually indicative of deficiency and those above 140 are usually considered normal.

Body Stores

The vitamin B_{12} stores of omnivorous healthy subjects are of the order of 4 mg (range 0.8-11.0), the majority being in the liver. It is lost from the body in an exponential fashion, the lower the stores the less the daily losses (9, 11, 12). By isotopic studies the half-life of vitamin B_{12} in man has been variously estimated to be from 480 (12) to 1360 (11) days, which by extrapolation indicates a loss of 0.2 to 0.07% of the stores per day. Normal stores in non-vegetarian subjects provide enough to prevent the development of overt deficiency for up to 2-10 years after intestinal absorption is interfered with (13).

Deficiency

Deficiency of vitamin B_{12} may arise either from prolonged inadequate dietary intake (*e.g.*, by young children breastfed by mothers deficient in the vitamin or in strict vegetarians) or because of some disease or state that interferes with its absorption (*e.g.*, gastrectomy, pernicious anaemia, disease or resection of the ileum).

The manifestations of vitamin B_{12} deficiency in man include an increased urinary excretion of methylmalonic acid; megaloblastic anaemia; changes in the epithelial cells of the gastrointestinal, urinary and genital tracts; neurological disorders from demyelination of peripheral nerves, optic nerves, spinal cord or brain; and in pigmented subjects, hyperpigmentation of the skin.

Recommended Intakes

Adults

The minimum body content of vitamin B_{12} necessary to maintain health is not known. In a group of patients with malabsorption of the vitamin who were given parenteral therapy to correct all evidence of haematological abnormality and to maintain the serum concentrations in the lower range of normal, the mean body store was 525 μg (14). If loss from this store occurs at the rate of 0.07 to 0.2% per day, an amount of 0.4 to 1.0 μg must be absorbed per day to maintain the store constant.

Adults with pernicious anaemia in relapse show a suboptimal haematological response to a parenteral dose of 0.1 μg of vitamin B_{12} (15). A parenteral dose of 0.5 to 1.0 μg will meet the daily requirement of patients with pernicious anaemia (16). Since these subjects have a deficiency of intrinsic factor, the vitamin excreted in the bile is not reabsorbed and their requirement for it is therefore greater than that of normal subjects.

In a small group of otherwise normal subjects with vitamin B_{12} deficiency of dietary origin in southern India, amounts of 0.3-0.65 μg in food produced satisfactory haematological responses although serum concentrations remained below normal (17).

The above observations and findings suggest that an intake of 1 μg of vitamin B_{12} per day will prevent the appearance of clinical manifestations of deficiency in the majority of individuals but will probably maintain body stores at only low levels. To allow for variations in absorption and other factors, including the maintenance of moderate body stores, an intake of 2 μg/day is recommended.

Pregnancy and Lactation

During pregnancy, vitamin B_{12} concentrations in serum fall (18). In the first half of pregnancy this is probably the result of an increase in blood volume and redistribution of the vitamin rather than a deficiency. In the latter half, the mother must also supply the vitamin B_{12} required for the fetal stores, which is approximately 0.3 μg/day (19). It is also possible that the increased metabolic demands of pregnancy may increase the requirement for the vitamin. An additional intake of 1 μg/day is recommended throughout pregnancy.

During lactation an average of 0.3 μg of vitamin B_{12} is excreted daily in breast milk (20). An additional intake of 0.5 μg/day is therefore recommended throughout lactation.

Infants and Children

The developing fetus *in utero* is dependent on transplacental transfer of vitamin B_{12} from the mother. This occurs preferentially, the concentration of the vitamin in the cord blood being higher than that in the maternal blood (21). At term, the fetus normally has 20-30 μg stored in the liver (19). If the mother should suffer from vitamin B_{12} deficiency during pregnancy these stores may be reduced (20). After birth the infant is dependent on its body stores and the amount supplied in its mother's milk. The concentration of viamin B_{12} in breast milk parallels that in the serum, therefore mothers deficient in it will provide milk with a low content (20). Infants suckled by these mothers may develop a severe vitamin B_{12} deficiency characterized by megaloblastic anaemia, developmental regression and involvement of the central nerv-

ous system. Such infants show a full therapeutic response to the daily oral administration of 0.1 μg of the vitamin (22). To allow for maintenance of stores, for growth and for individual variability, an intake of 0.3 μg/day is recommended for infants. This quantity should be increased progressively with increasing body size until the level of the intake of adults is reached.

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Biotin

Biotin is known to be particularly involved in carboxylation reactions (1) and in its absence all of those reactions appear to be affected. It has also been implicated in a number of reactions in the metabolism of carbohydrate, fat and protein (2). Bonjour (3) has recently reviewed the role of biotin in human physiology, and metabolic disorders responsive to biotin in man have also been recently investigated (4, 5).

Symptoms of deficiency can be produced by dietary restriction but usually a deficiency is produced by the ingestion of a large quantity of avidin, which combines with biotin and prevents its absorption

from the gut (6-8). The biotin content of the usual diet has been estimated by Oppel (9) to be 30-40 μg/day and by Williams (10), 14 μg/day. Bonjour (3) cites statistics indicating a biotin intake of 70 μg per person per day for the Swiss population and 50-100 μg/day in the usual European diet. Besides dietary sources of biotin, man obtains an unknown quantity from microbial synthesis in the gastrointestinal tract (3).

Biotin is excreted in both faeces and urine. Bonjour (3) proposes that the faecal excretion is a measure of synthesis by bacteria in the gut and that the urinary biotin reflects the dietary intake. The total amount excreted is greater than the total dietary intake (3), with urinary biotin levels less than the intake. Oppel (9) reported a level of 116 μg/24 h in faeces and 46 μg/24 h in urine. This level in urine was the highest amount cited by Bonjour (3), based on information from several studies.

Denko et al. (11) found that the level of biotin in whole blood and the amount excreted in the urine were not affected when subjects were changed from a diet containing 44 μg/day to one containing 20 μg/day and maintained at that level for 15 weeks.

A dietary intake of 1.5 μg/kg of body weight per day has been suggested for all age groups. The intake per day for the adult would be about 100 μg, which falls within the upper range of usual intakes (3, 10). This amount would readily meet the estimated daily losses of the vitamin in the urine (3). Mature human milk contains 4 μg/L, thus an infant consuming an average of 750 mL/day would receive about 3 μg/day from that source. Calculated on the basis of 1.5 μg/kg of body weight, the suggested intake for the infant would be about 10 μg/day. There is no indication that breast milk is inadequate. It would appear that 1.5 μg/kg per day is well above the actual requirements of infants and perhaps of adults. No definite estimate of requirements can now be made.

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Pantothenic Acid

Pantothenic acid is a component of coenzyme A. As such it is involved in cellular respiration and thus in the intermediary metabolism of carbohydrate, lipid and protein (1). As the 4-phosphopantotheine moiety of acyl carrier protein it is involved in the synthesis of fatty acids.

The usual mixed diet provides 5-20 mg of pantothenic acid per day (2-6), amounts that are considered adequate to meet nutritional requirements. Johnson and Nitzke (7) found that the average intakes of two groups of women with low incomes were 4.0 and 4.2 mg/day, and there were no clinical signs of deficiency.

Fry *et al.* (8) studied the metabolic response of male prisoners to a diet deficient in pantothenic acid. They found that a dietary intake of approximately 7 mg/day produced a urinary excretion of about 3 mg/day. The urinary levels decreased when the vitamin was removed from the diet and increased with supplements of 10 or 100 mg/day. Tao and Fox (9) reported a mean excretion of 2.7 mg/day by acute alcoholics. Normal subjects eating *ad libitum* have been reported to excrete 3.8 mg

of pantothenic acid per day (10). Srinivasan and Belavady (11), in a study of the pantothenic acid status of several groups of women in India, estimated that non-pregnant women consuming diets based on cereals that provided 3-4 mg/day excreted an average of 2.5 mg/day. They suggested that this level of excretion indicated a marginal level of adequacy of intake. Cohenour and Calloway (12) reported that the daily food records of 17 pregnant teen-age girls showed that their mean intake was 4.7 mg of pantothenic acid per day, which they thought might reflect intakes of less than the usual amounts. The pregnant women studied by Srinivasan and Belavady (11), whose intakes were 3-4 mg/day, excreted an average of 2.0 mg/day, not significantly different from the amount excreted by the non-pregnant women. There were no clinical problems that could be attributed to the nutritional status with regard to pantothenic acid. Other studies have shown that intakes of approximately 1.0 mg/day for 3-18 months have not produced clinical symptoms (13-15). Symptoms of deficiency have been produced by ingestion of the metabolic antagonist ω-methylpantothenic acid (16-20).

The pantothenic acid content of self-selected diets chosen by adult subjects who participated in several studies was approximately 7 mg/day, or 2.3 mg/1000 kcal (2.7 mg/5000 kJ) (6,8,9). On this basis, 5-7 mg/day appears to be suitable for the adult.

Mature human milk contains about 2 mg of pantothenic acid per litre, so an infant consuming an average of 750 mL daily would obtain 1.5 mg of the vitamin per day. This amount compares favourably with a suggested intake of 1.6 mg/day calculated on the basis of 2.3 mg/1000 kcal (2.7 mg/5000 kJ). An intake of 2 mg/day, which takes variability into account, is appropriate for the infant.

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VIII. MINERALS

Calcium and Phosphorus

Calcium

Calcium is unique among the nutritional elements in the extent to which it is concentrated in certain body tissues and in certain foods. About 99% of the calcium in the body is present in the skeletal tissues. It is found in high concentrations in only a limited number of foods (mostly of dairy origin), and hence the calcium intake is markedly dependent upon a few food items. The requirement for calcium cannot be defined with the degree of precision that applies to most other nutrients because the body adapts to a range of intakes by regulating the excretion in the urine and the efficiency of absorption from the intestine. Consequently, frank deficiency of calcium is rarely seen in human subjects.

The 1% of body calcium that is not concentrated in the skeleton is involved in numerous metabolic processes, including enzyme activation, hormone function, nerve transmission, blood clotting and membrane transport. Calcium metabolism is affected by several hormones that regulate its absorption from the intestine, mobilization from the skeleton and reabsorption from the kidney tubules. The concentration of calcium in the serum is homeostatically regulated within a very narrow physiological range and deviations from that range may have severe functional consequences.

The amount of calcium absorbed by adults can be expressed as a curvilinear function of the intake, increasing rapidly with the intake up to about 10 mg/kg of body weight per day and then only moderately (1). Conversely, what is called the percentage true absorption (intake minus faecal excretion corrected for endogenous faecal calcium, expressed as a percentage of the intake) decreases rapidly as the intake increases up to 10 mg/kg of body weight per day, then declines slowly with further increases in the intake. At an intake of 15 mg/kg per day, about 11 mg of calcium are excreted in the faeces (2 mg from endogenous sources) and 4 mg in the urine. From this intake the total amount absorbed per day is approximately 7 mg/kg of body weight, which includes the reabsorbed portion from digestive juices, about 3 mg/kg per day (1).

A decrease in the intake of calcium causes a mild depression in the

level in serum and a consequent increase in the synthesis of parathyroid hormone. This hormone stimulates the reabsorption of calcium from the renal tubules and the formation of 1,25-dihydroxycholecalciferol in the kidney (2). This hormonal form of vitamin D stimulates the uptake of calcium from the intestine by a mechanism that apparently involves the synthesis of protein(s) required for the active transport of calcium, thereby enabling the body to re-establish calcium balance following a decrease in the intake (3). There are indications, however, of variability in the capacity to regain calcium balance under conditions of a reduced intake (4).

The recommended intake of calcium for the term infant during the first 6 months of life is influenced by the generally accepted view that the requirement during this period is fully met by the normal amount of breast milk from healthy mothers. A typical production of 750 mL/day provides 250 mg of calcium. About two-thirds of this amount is retained by the infant. In consideration of the variability in the secretion and intake of breast milk, the requirement, including allowance for variability, would be about 325 mg/day.

Cow's milk contains 3.5 times as much calcium and 6.6 times as much phosphorus as human milk (*i.e.*, about 1170 mg of calcium and 920 mg of phosphorus per litre, Ca:P 1.27:1) (5). The high phosphorus content of unmodified cow's milk is unfavourable for human neonates since it depresses serum calcium, stimulates the synthesis of parathyroid hormone and the resorption of bone, and poses a risk of tetany. Typical formulae made from cow's milk with added carbohydrate contain concentrations of calcium and phosphorus that are about 1.5 and 2.8 times, respectively, the concentrations in breast milk (*i.e.*, about 500 mg of calcium and 400 mg of phosphorus per litre). A proportionately lower fraction of these elements is retained by the infant.

The recommended intake of calcium is 350 mg/day for infants during the first 6 months of life, which is higher than the average intake of breastfed infants. It allows for the greater requirement of rapidly growing infants and for the increased calcium needed to balance the higher intake of phosphorus from modified cow's milk formulae. Breast milk satisfies the calcium needs of term infants but it does not contain sufficient calcium to sustain the rate of skeletal mineralization in premature infants that normally occurs *in utero* (6).

Low intakes of calcium are associated with a decreased rate of skeletal development in children, but it is not known whether there are any lasting consequences such as a decrease in bone mass in adulthood. The increments in recommended intakes during growth reflect increasing requirements for skeletal maintenance and accretion. The calcium requirement of the two sexes is similar until the

earlier pubertal growth spurt in girls temporarily raises their requirement above that of boys. Thereafter the smaller skeletal mass of females imposes a lower requirement. Beyond 50 years of age, however, the recommended intake for women is raised to that for men because of evidence that a liberal intake of calcium decreases their greater susceptibility to loss of bone during aging (7). Increments in retention during pregnancy and the secretion of up to 325 mg/day during lactation are reflected in recommended intakes of 500 mg/day above maintenance. The efficiency of calcium absorption is enhanced during the second and third trimesters of pregnancy and during lactation (1).

Much attention has been focused on a possible relationship between the intake of calcium during adult life and susceptibility to osteoporosis, the most prevalent disease of the skeleton in the aged. Although there is no obvious relationship between the calcium content of national food supplies and the incidence of osteoporosis, there are indications that the calcium requirement of populations consuming an acidic western diet high in protein and phosphorus is higher than that of populations consuming a cereal based diet. A recent study on two populations of Yugoslavian adults differing markedly in their intakes of calcium (400-500 vs. 800-1000 mg/day) disclosed that the lower intake was associated with decreased cortical bone mass in young adults and increased rate of femoral fracture in the aged (8). There is considerable evidence that the intake of calcium during early adulthood has an influence on bone mass in middle age, which appears to be the main determinant of bone mass in the elderly (9). Although calcium supplementation has been found to be of limited value in reversing the loss of bone associated with osteoporosis, a liberal intake decreases the rate of osteopenia that follows the menopause and thereby reduces the risk of bone fracture (7).

Controlled studies on adult subjects have shown that diets high in protein (about 140 g/day) are associated with an increased excretion of calcium in the urine (10). The absorption of calcium is slightly increased but this does not fully compensate for the increased excretion, consequently there is a loss of calcium from the skeleton. Calcium balance can be restored by increasing the intake. High protein calciuria appears to be due primarily to an increased load of metabolic acid, as sulphate, that is produced by the oxidation of excess sulphur amino acids (11). When the intake of phosphorus is increased along with protein, however, as is the case in normal food selection, the hypercalciuric effect of the protein is offset by the hypocalciuric effect of the phosphorus (12). The long-term implications of these findings are still not clear.

Data on the nutrient contribution of major food groups to the

Canadian food supply for 1975 indicate that 76% of the total calcium available was supplied by dairy products (13). The average daily consumption of calcium exceeded the recommended intakes at most ages but the mean intakes of older adults, especially women, were below the recommendations (14). Calcium consumption by native peoples was below the national average (15, 16). Because of wide variability in the use of milk and other dairy foods, average values for older adults conceal the fact that many individuals in this age group consume 500 mg of calcium or less per day.

The recommended intakes of calcium for adults vary from 700 to 900 mg per day (See Table X.I.).

Phosphorus

About 80% of the phosphorus in the adult body is in the skeletal tissues where it is present in hydroxyapatite crystals in a Ca:P ratio of approximately 2:1. The rest is in soft tissues as inorganic phosphate and as a constituent of all of the major classes of biochemical compounds: proteins, lipids, carbohydrates, enzymes and nucleic acids. The energy that drives most metabolic processes is derived from the phosphate bonds of ATP and other high energy phosphate compounds.

The ubiquitous presence of phosphorus in foods ensures an adequate dietary intake. Consequently little attention has been given to the consumption of phosphorus until recently. The possibility that the human requirement for calcium may be affected by the intake of phosphorus, however (as it is in animals), has stimulated an interest in intakes of phosphorus and in the ratio of dietary calcium to phosphorus.

Most human foods contain more phosphorus than calcium, the main exceptions being green vegetables and dairy products. These food groups nevertheless provide 40% of the phosphorus available from the major food groups in Canada (13). Food disappearance data indicate that in 1975 there were 965 mg of calcium and 1510 mg of phosphorus per person per day available for consumption by Canadians (Ca:P 1:1.57) (13). A composite Canadian diet in 1972 was estimated to contain 1600 mg of phosphorus (17). If related to the weighted value for the intake of calcium *per capita* derived from the Nutrition Canada survey (14), 950 mg, this estimate yields a Ca:P ratio of 1:1.68. A ratio of 1:1.6 was calculated for the Canadian diet in 1971 (18).

Despite these relatively consistent estimates of average calcium and phosphorus intakes of the national population, it is apparent that the intakes of both are highly variable and depend upon the consumption of foods such as meat and eggs that are high in phosphorus and low in calcium, the intake of phosphorus in food additives and the

consumption of dairy products (which provide 76% of the available calcium) (13). This variability is evident in the results of a study of the intakes of calcium and phosphorus by a group of Canadian university students (19). The average amounts of 880 and 1590 mg/day (Ca:P 1:1.8) are both marked by large standard deviations (397 and 806 respectively).

The estimated average calcium intake of 600 mg/day by Canadian women aged 40-64 years (14) indicates a low consumption of dairy foods by this group. Since the Ca:P ratio in dairy products favours calcium, a low intake of these foods diminishes the dietary Ca:P ratio. Experiments on adult rats, mice and pigs have indicated that the chronic feeding of a diet with a Ca:P ratio lower than 1:2 is associated with reductions in bone mass (18, 20). This is due to a decrease in the serum calcium concentration caused by the flux of excess phosphorus through the blood, resulting in bone resorption induced by a stimulation of parathyroid hormone (21, 22). The importance of the Ca:P ratio diminishes with the phosphorus intake, however, and since dairy foods are high in phosphorus as well as in calcium, any adverse effect of a lowering of the Ca:P ratio occasioned by a low consumption of these foods may be modulated by the concomitant reduction in the total intake of phosphorus.

A typical daily output of 750 mL of mature breast milk contains 105 mg of phosphorus (5), which appears to be adequate to meet the needs of the nursing infant. The intake is higher than this by infants fed typical modified cow's milk formulae, which contain 330-450 mg/L. Unmodified cow's milk contains more phosphorus (920 mg/L) (5) than is desirable for human neonates, as evidenced by an increased requirement for calcium to prevent depression of blood calcium and predisposal to tetany. Although breast milk contains less calcium than cow's milk (340 vs. 1170 mg/L) (5), the ratio of calcium to phosphorus in breast milk (2.36:1) is more favourable than that of cow's milk (1.27:1) and nursing infants show normal skeletal development when the flow of milk is adequate.

During the growing period the requirement for phosphorus, like that of calcium, is influenced mainly by the needs of the developing skeleton. There is little information on the requirements of phosphorus for growth, or for maintenance, pregnancy and lactation in the adult, but intakes of phosphorus equivalent to those of calcium may be considered adequate. The fact that there is more phosphorus than calcium in most common foodstuffs is assurance that the phosphorus requirement of healthy persons is met by all normal diets.

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Magnesium

Magnesium is the fourth most abundant cation in the body, amounting to approximately 25 g in the adult male (1, 2). Sixty per cent of it is in bone and 1% is extracellular. Approximately two-thirds of the latter fraction is ionized and biologically active. In both sexes and at all ages this extracellular fraction and the ratio of bound to unbound metal in it remain constant (3, 4), which indicates close homeostatic control.

Magnesium is a co-factor for all enzymes requiring ATP; and it is required for maintenance of the integrity of DNA and ribosomes and for the replication of DNA and the synthesis of RNA (3). It is involved in many phases of calcium homeostasis through a role in the release and function of parathyroid hormone. Hypomagnesaemia is almost always accompanied by hypocalcaemia (5). Deficiency of magnesium is manifested by weakness, failure to thrive, neuromuscular dysfunction, convulsions, tachycardia and fibrillation, and if unrelieved, results in coma and death (5, 6). An excessive intake of magnesium can result in impaired neuromuscular transmission mediated by diminution of endplate potentials (6, 7).

Absorption from the small intestine and excretion by the kidneys show adaptive responses that indicate major roles in magnesium homeostasis; and this situation contributes importantly to the difficulty of estimating nutritional requirements. The absorption of magne-

sium is related to the amount ingested and the length of time it remains in the small intestine (3). The results of studies with tracers have indicated that from diets that provide 23, 240 and 564 mg/day, absorption is about 75, 45 and 25% respectively (3). Absorption involves both passive diffusion (about 10%) and a facilitated process (8). Equilibration of magnesium in the body is slow (9). The results of studies of urinary excretion patterns of ^{28}Mg have suggested that there are four body pools. Three of the pools have half-lives of about 1, 3 and 14-35 h, and the last pool turns over at less than 2% per day and probably represents the magnesium in bone (9).

The excretion of magnesium is primarily through the kidneys, and less than 2% of endogenous magnesium is excreted in the faeces (3). Excretion in the urine increases when either dietary or parenterally administered magnesium increases. With a normal adequate diet the majority of the absorbed element is excreted. The maximum renal capacity is in excess of 2 g/day (3). When the intake is decreased, the kidney is very effective in conserving the mineral (10). It appears that the kidney is the primary regulatory site for magnesium homeostasis, with the gut playing a smaller but important role. Dermal losses are only about 15 mg/day in the adult (11).

Because of the homeostatic mechanisms it is very difficult to produce overt signs of depletion or excess of magnesium in normal humans (3). Depletion can occur in certain pathological conditions and in chronic alcoholism (6). Toxicity has been reported when the administration of magnesium has been undertaken during chronic renal failure and during therapy with magnesium salts (7).

From information on food consumption obtained in the Nutrition Canada survey, the following average intakes of magnesium (mg/day) have been calculated (12): children 1-4 years old, 204; 5-11 years, 260; boys and girls 12-19 years, 323 and 234 respectively; men and women 20-39 years, 302 and 206 respectively; men and women 40-64 years, 258 and 187 respectively; men and women of 65+ years, 221 and 174 respectively. The principal sources were cereals (27%), fruits and vegetables (27%) and dairy products (17%), with a much higher proportion from dairy products for children. There is no indication that these levels of intake are inadequate for the Canadian population.

Requirements and Recommended Intakes

Adults

Three general approaches to the estimation of requirements of adult people for magnesium are possible: (i) calculation of minimum dietary needs under fully adapted conditions in the intestine and kidneys (see preceding discussion); (ii) observation of usual intakes in a free-living population; (iii) balance studies, with the recognition that

this approach presents problems concerning duration. Physiological data suggest that under conditions of low intake, the kidneys can conserve up to about 12 mg/day (10). The faecal loss of endogenous magnesium is apparently small, amounting to about 2% of a parenterally administered amount, and the dermal loss is about 15 mg/day. This information suggests that the need for absorbed magnesium under adapted conditions might be much less than 50 mg/day and that at low levels of intake absorption would be more than 50%. A very conservative estimate of requirement for the adult, therefore, would be below 100 mg/day. As noted above, average intakes calculated for young adult men and women were 302 and 206 mg/day, which are equivalent to about 4.0 and 3.5 mg/kg of body weight per day.

The results of balance studies, particularly early studies, have suggested that requirements are relatively high; but the interpretation of balance studies is difficult because of the adaptive processes and relatively long equilibration periods that have been discussed above. In one study (13), men and women ate diets that provided 2.0-4.7 mg/kg of body weight per day and each subject was tested on only one level of intake. At intakes below 2.9 mg/kg, only two of nine subjects approximated or exceeded balance; at 3 mg/kg, two of three subjects approximated or exceeded balance; above 3.4 mg/kg, all approximated or exceeded balance (only subjects who were observed for 6-9 days after a 3-day preliminary feeding period are included). These observations suggest that the average requirement for balance under the conditions of the experiment was about 3 mg/kg per day and that an intake of 3.4 mg/kg per day was adequate for all. This is reasonably consistent with the observation that with average intakes of 3.5-4.0 mg/kg per day by Canadian adults there is no indication of deficiency among normal people.

On the basis of these observations, the recommended intake of magnesium for young adults of both sexes is 3.4 mg/kg of body weight per day. The requirement probably is related to lean body mass, so that obese people would have a lower requirement on the basis of body weight (13). In the absence of information to the contrary, this level is recommended also for older adults, although it should be noted that it is above the observed average intake.

Infants and Children

During periods of rapid growth of tissue and bone it would be expected that the requirement for magnesium per unit of body weight would be high compared with that of adults (14), but specific data on which estimates can be based are not available.

Human milk provides about 6 mg of magnesium per 100 kcal (420 kJ) (15). A newborn infant would ingest an average of about 21 mg/day,

about 7.2 mg/kg. At 4 months of age the calculated intake from breast milk would average a little less than 6 mg/kg per day. These levels of intake are taken as adequate to meet the needs of almost all infants. The recommended intake is 7 mg/kg per day in the first 3 months, 6 in the next 3 months and then amounts progressively falling to about 4.5 mg/kg per day for older children and adolescents and 3.4 mg/kg per day for young adults.

Pregnancy and Lactation

During pregnancy the maximum rate of accretion of magnesium in the fetus is about 8 mg/day (16). If approximately 45-50% of the magnesium in the mixed Canadian diet is absorbed (3, 12), the increased dietary requirement for fetal deposition would be about 16 mg/day. If there are also increases in requirements for placental and maternal tissues, as well as variability among women, the recommended intake for the third trimester of pregnancy is 25 mg/day above that for the non-pregnant woman. A lower level would suffice in early pregnancy.

If it is accepted that the magnesium content of breast milk is 6 mg/100 kcal (1.4 mg/100 kJ) (15) and that at full lactation the average secretion is equivalent to 525 kcal/day (2205 kJ/day), with a coefficient of variation of 15%, the secretion of magnesium, including an allowance for variability, would be 40 mg/day. On the assumption of 50% absorption, the recommended intake for lactating women is 80 mg/day above that for non-lactating women.

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Iron

The major compartments of iron in the body are: circulating haemoglobin; the storage forms ferritin and haemosiderin; small amounts in the plasma associated with transferrin, the transport protein, or in ferritin; small but biologically very important amounts in myoglobin and enzymes in the tissues. Total amounts of body iron are lower in women than in men. The amounts of myoglobin and enzymes in tissues are probably proportional to body weight in both sexes. Haemoglobin mass is lower in the female, which is a true physiological difference. Iron stores are also appreciably lower in women than in men (1), which is the result of characteristic differences in the adequacy of the intake in relation to the requirement for iron between men and women. The condition has been termed iron depletion and is thought to be relatively widespread among women in North America. Deficiency in iron, a more severe state, is usually characterized by microcytic hypochromic anaemia. Relatively little is known about the functional level of the iron containing enzymes in iron depletion and deficiency. There is wide disagreement about the symptomology to be expected in states of iron depletion and deficiency (2, 3).

Estimates of iron requirements are based upon the amounts of

dietary iron required to establish and maintain a reasonable level of storage rather than merely enough to prevent anaemia or other clinical symptoms. As depletion and deficiency of iron develop consequent to a low dietary intake, certain adaptations by the body (such as increased efficiency of absorption) take place that potentially establish a new equilibrium at a lower plane of nutritional status. Conversely, as intakes of iron increase above levels of requirement, the body adapts by decreasing the efficiency of absorption, so that in this case also a new state of equilibrium is achieved but in the presence of a higher level of iron storage. This is typically the case in men as compared to women. The overall regulation of levels of body iron is governed chiefly by the absorptive process of the gut. This is in contrast to many other nutrients, for which homeostasis is regulated in large part by the kidneys. This phenomenon presents particular problems in the estimation of requirements since it is necessary to define the target nutritional status and to establish the efficiency of absorption, a regulated process, to be expected at that level of body nutriture. The situation is further complicated by the fact that the proportion of dietary iron that is availabie for absorption, sometimes called the bioavailability, is affected by the nature of the diet. In general, diets rich in foods from animal sources are associated with a high bioavailability and hence a lower requirement for dietary iron, and diets rich in cereal foods are associated with a low bioavailability and a higher dietary requirement (2-7); therefore dietary requirements for iron must be expressed in terms of particular types of diets.

The Need for Absorbed Iron

Iron is lost from the body through the intestine, in the urine and via the skin, and in women, also in the menstrual fluids. The faecal and dermal losses include both secreted iron and actual loss of epithelial tissues that contain it. From experiments with radioisotopes, the total daily losses of iron through all routes by adult males have been reported to range from 0.9 to 1.0 mg (8). In a group with very high iron stores, approaching what may be called iron overload, the observed total loss was about 2 mg/day, so that to some degree losses are related to the amount of stored iron. On the basis of body weight, adult males with normal iron stores excrete about 14 μg/kg per day. On this basis the predicted loss by adult women would be about 0.77 mg/day and that of infants 6-9 months old about 0.11 mg/day. If it is assumed that losses are related to the basal metabolic rate (BMR) (and to body weight expressed as $kg^{0.75}$), the loss by the adult male would be about 0.52 μg per basal kilocalorie (0.12 μg per basal kilojoule). By extrapolation, the loss by the adult female would be 0.67 mg/day and that for the infant, 0.12 and 0.23 mg/day at 1.5 and 7.5 months respectively. There

are few direct data for women, and either of the above estimates would be consistent with total losses by menstruating women measured by the use of radioactive iron (9). Garby *et al.* (10) reported faecal losses of about 0.25 mg/day in infants. These values are very close to the total losses suggested by the model adjusted to the BMR and much higher than those predicted from the assumption of a linear relation to body weight. In the infant, intestinal losses may be increased by the feeding of cow's milk (loss in occult blood) (11). In the absence of more precise data, it is assumed that basal losses of iron in children, adolescents and adult women are proportional to the BMR. Estimates so calculated are presented in Table VIII.1. In the case of infants, total losses have been assumed to be somewhat higher than those predicted on the basis of BMR.

At birth, the iron content of an infant of normal weight and term is about 80 mg/kg, or a total of 270 mg (12). After 3 months there is little change in the total amount but there has been major redistribution. The fall in haemoglobin during this period is physiological. Thereafter the total amount of iron in the body, including that in the haemoglobin mass, increases steadily with growth. Failure of the haemoglobin concentration in the blood to rise in older infants is suggestive of dietary inadequacy. Hawkins (13) has suggested that at 12 months of age the total body iron is about 400 mg, which implies an increase of about 0.5 mg/day after 3 or 4 months of age. This estimate is in reasonable agreement with more recent estimates of 0.3-0.7 mg/day during this period (2, 14).

In the male North American at age 30, iron stores may average about 1000 mg (2); but they are much lower in the female. This is a function of the intake of iron in relation to the need. To develop estimates of requirement, it can be assumed that storage levels found in the free-living population are the desired levels, or a normative standard can be adopted. The former approach would imply that iron depletion in women is desirable, and so is rejected. A target iron storage of 500 mg for both men and women is adopted, which is the level assumed by an FAO/WHO committee (4). Accordingly, between 4 months and 20-25 years of age the individual would be expected to accumulate about 500 mg of storage iron as well as that included in the progressively increasing haemoglobin mass and functional compartments in tissues and plasma.

Hawkins (13) developed a model of iron accretion during growth from infancy to adulthood based upon consideration of rate of growth and calculated changes in haemoglobin mass. The figures in Table VIII.1 for groups from 1 year of age to adulthood have been recalculated after his model of increments in haemoglobin mass and tissue iron (functional plus stores), the final target being 500 mg of storage iron for

both sexes. The body weights used by Hawkins do not coincide exactly with those that have been recorded in Canada more recently but the difference in projected requirements for iron is small and has been ignored.

By adding together the predicted basal losses and the predicted accretion of iron, an estimate of the *average* requirement for *absorbed* iron (excluding menstrual loss in females) is obtained. It is to be expected that there would be individual variability in the actual needs for iron. The magnitude of this variability in basal needs is not known. If it is accepted that growth rate may be a major variable, the coefficient of variation might be about 15%. A similar figure would be obtained by considering the variability of birth weight, a determinant of the initial iron content of the body. For purposes of the present estimates of iron needs, a coefficient of variation of 15% is accepted and the average requirement is increased by a factor of 1.3 to form the basis of the recommended intakes expressed as absorbed iron.

For females after puberty, provision must be made for the iron in menses. Menstrual losses are quite consistent in individual adult women from one cycle to the next, but there is wide variation among women and the distribution of losses shows a marked skewing. The average loss, estimated over the whole menstrual cycle, is about 0.63 mg/day. The observed distribution of losses is: median, 0.45 mg/day; 90th percentile, 1.35 mg/day; 95th percentile, 1.75 mg/day (5). To derive a recommended intake intended to cover the needs of almost all individuals the 95th percentile figure has been used. In adolescent girls, menstrual iron losses are initially somewhat lower than those of adult women. Hallberg *et al.* (15) reported that the 95th percentile of loss in adolescents is about 1.4 mg/day. These figures have been incorporated into those in Table VIII.1. It is assumed that menstruation begins at 13 years of age, but of course this varies among individual girls. In interpreting the derived recommended intake, it should be recognized that the two factors that exert major influences on iron requirements during these years are the pre-menarchal growth spurt and the onset of menstruation. Requirements will be high as a result of each. They are sequential, not concurrent. Depending upon the individual girl and her pattern of maturation, the suggested figures for those 10-13 years old could underestimate the actual requirements and the figures for those 13-16 years old could overestimate them.

The Absorption of Iron from Foods

The absorption of iron is a regulated process responsive to the iron nutriture of the subject and to his or her need for iron. Cook *et al.* (16), using plasma ferritin as an index of body iron stores, demonstrated an inverse relationship between the logarithm of plasma ferritin and the

percentage of food iron absorbed (range of mean levels of plasma ferritin, 8-45 μg/L; range of mean iron absorption, 4-45%). Increased absorption in subjects with anaemia from iron deficiency has been repeatedly demonstrated; and absorption is also affected by the rate of erythropoiesis (17-19). The status of iron stores seems to be a dominant influence. Among people with comparable stores, the body's need for iron is a determinant of iron absorption; that is, within the range of degrees of absorption that have been observed even after attempts to standardize for iron status, it is assumed that there is a positive correlation between absorption and need.

The nature of the diet affects the relative availability of iron for absorption. When single foods are studied, the absorption from plant foods, particularly cereals, is much lower than that from meat, poultry and fish. Furthermore, there are interactions among foods in a mixed diet. The presence of foods from animal sources stimulates the absorption of iron from plant sources and there is a small reverse effect in the opposite situation. The presence of ascorbic acid stimulates the absorption of iron, and a number of other chemicals, natural constitutents of or intentional additives to foods, have been shown to influence it. There are two pools of iron in the gut, haem and non-haem iron. When several foods are eaten concurrently the iron from them forms common pools within the lumen of the gastro-intestinal tract. Iron added to foods behaves in the same manner as iron present within them (20, 21) if it is in a soluble form. This has significance when the absorption of iron added to foods for fortification is considered. Standards of solubility have been proposed for iron for such use (22). The two iron pools behave quite differently with regard to the effect of the composition of the diet. The absorption of haem iron is generally high and is relatively unaffected by the nature of the diet, whereas the absorption of non-haem iron is generally lower and is markedly affected by the composition of the diet (2). The results of these effects are referred to as the bioavailability of dietary iron.

The degree of absorption of iron from the diet is the result of the interaction of corporal (iron stores, iron need) and intraluminal (dietary composition, level of dietary iron) factors. For a given state of iron nutriture and body need, bioavailability influences the actual absorption, and for a given mixture of food, absorption is determined by nutritional status and body need. Because of this interaction, it is difficult to predict the degree of absorption that must be considered in the estimation of requirements. The preferred approach would be to define the proportion of dietary iron that could be absorbed by an individual with the accepted level of iron stores (500 mg in the adult), who has the highest individual need and who consumes a diet that contains the minimally adequate amount of iron and the expected

mixture of foods. This would constitute a prediction of the upper limit of iron absorption appropriate to the estimate of the need for absorbed iron expressed as the average need plus an allowance for variability of requirement. Unfortunately, this is not the way in which information on absorption has been reported in the literature. The customary method is to describe the *average* absorption by so-called normal individuals, which for men would imply that there is a store of about 1000 mg. This would clearly underestimate the degree of iron absorption that would be expected in the case of the individual described above.

The FAO/WHO committee (4) approached this problem by examining in detail sets of data on iron absorption and selecting individuals who appeared to have traits consistent with the situation described above. The committee also looked at the range of absorptions reported in chemical balance studies in which mixed diets were consumed. From these examinations a judgment was reached that the probable upper limits of iron absorption in non-depleted subjects are as shown in Table VIII.2.

The average pattern of food consumption reported in Nutrition Canada (23) suggests that meat, fish, poultry and eggs together contribute about 24% of the food energy for adults (milk products contribute 11%) and 14 and 17% of that for children and adolescents (milk products, 19 and 16%). By the FAO/WHO guideline, this suggests that the assumed iron absorption should be 20% or, if milk products are excluded, 15%.

Monsen *et al.* (7) have recently published a model for the prediction of the *average* absorption of iron from single meals, the use of which attempts to take into account body stores of iron, body needs for iron (male *vs.* female) and the amounts of meat and ascorbic acid in the meal. It is not intended that this model be applied to average data for populations, but it seems to imply an average absorption below 10% when fitted to information on food consumption from the Nutrition Canada Survey.

In the Dietary Standard for Canada published in 1975, it was assumed that the *average* iron absorption was about 10% (somewhat higher in menstruating females). This was based upon a review of reported mean absorptions ranging from as low as 1% from rice to 20% from veal muscle (24). A high variability of absorption was noted. At that time the *average* absorption was applied to the *average* need for absorbed iron to derive recommended intakes.

If *average* figures for absorption, either as used in the Canadian standard of 1975 or as predicted by the model of Monsen *et al.* (7), are applied to the estimates of requirements for absorbed iron including provision for variability, as shown in Table VIII.1, the recommended intakes for men seem reasonable in relation to usual dietary intakes,

but those for women and young children are totally inconsistent with experience. Conversely, if the FAO/WHO estimates of the upper limit of absorption are applied, the recommendations so derived are consistent with experience (5); that is, the predicted prevalence of women with intakes below their actual requirements seems consistent with the observed prevalence of iron depletion. It is thus suggested that an upper limit of absorption approximating 20% should be applied to menstruating women. Although the same figure would seem to be appropriate for adult men with iron stores of only 500 mg, it is also rational to suggest a more conservative estimate of absorption for men in recognition that the normal situation would involve a higher level of storage. Such a difference between males and females and recognition of higher levels of iron stores would be consistent with the model of Monsen *et al.* (7). Young children undergoing rapid growth might be expected to be more similar to women than to men with respect to the absorption of iron. These considerations have been applied in the derivation of the dietary intakes shown for children and adults in Table VIII.1.

Iron Requirements of Infants

Estimates of the need for absorbed iron during infancy are presented in VIII.1. These may be overestimated. Breast milk has been reported to have an initial iron concentration of about 0.6 mg/L that falls to about 0.3 mg/L after 5 months (25, 26). Other reports have given concentrations ranging up to 1 mg/L or more (27, 28). During the first months of life, the intake of iron from this source must be quite low and certainly well under 1 mg/day. Human milk is notable for the very high bioavailability of its iron (27). Experience suggests that these low intakes that breast milk provides are adequate to meet the needs of the infant through 4-6 months. The suggested intake is based on the assumption that the iron is obtained from breast milk that provides enough for a full-term infant in rapid growth. In 1971 a dangerous prevalence of low haemoglobin levels was discovered in some groups of Canadian infants over 6 months of age (29). It would appear that cow's milk formulae and cereals for infants that were fed at that time provided insufficient iron to meet the needs of many infants. It is to be noted that this may not be the present situation. The iron that is added to cereals for infants now is in a preparation that is known to be soluble and hence available for absorption, which may not have been true at the time when anaemia was prevalent.

These observations imply that when the infant is weaned from the breast both the intake and bioavailability of iron in the mixture of foods

Table VIII.1.
Derivation of Recommended Intakes of Iron

Age	Sex	Basal Loss (mg/day)	Expected Accretion (mg/day)	Basal Loss + Accretion: Average (mg/day)	Basal Loss + Accretion: Including Variability (mg/day)	Menstrual Loss (mg/day)[a]	Intake Recommended (mg/day)
Months							
0-2	Both	0.20		0.20	0.26		0.4[b]
3-5	Both	0.25	0.30	0.55	0.71		5
6-8	Both	0.30	0.50	0.80	1.04		7
9-11	Both	0.32	0.50	0.82	1.07		7
Years							
1	Both	0.30	0.38	0.68	0.88		6
2-3	Both	0.34	0.29	0.63	0.82		6
4-6	Both	0.42	0.28	0.70	0.91		6
7-9	M	0.53	0.37	0.90	1.17		7
	F	0.49	0.38	0.87	1.04		7
10-12	M	0.64	0.58	1.22	1.59		10
	F	0.61	0.61	1.22	1.59		10
13-15	M	0.76	0.80	1.56	2.03		12
	F	0.71	0.12	0.83	1.08	1.40	13
16-18	M	0.86	0.25	1.11	1.44		10
	F	0.75	0.10	0.85	1.11	1.40	14

Table VIII.1.
Derivation of Recommended Intakes of Iron

Age	Sex	Basal Loss (mg/day)	Expected Accretion (mg/day)	Basal Loss + Accretion		Menstrual Loss (mg/day)[a]	Intake Recommended (mg/day)
				Average (mg/day)	Including Variability (mg/day)		
19-24	M	0.95	0.02	0.97	1.26		8
	F	0.67	0.10	0.77	1.00	1.75	14
25+	M	0.95		0.95	1.24		8
	F	0.67		0.67	0.87	1.75	14[c]
Pregnancy (recommended intake 6 mg/day additional)[d]							
Lactation (recommended intake same as that for the menstruating woman)							

[a] 95th percentile.
[b] Assumption that breast milk is the source of iron for the first 2 months and a mixed diet thereafter.
[c] After the menopause the recommended intake is 7 mg/day.
[d] Assumption that iron stores are low before pregnancy.

Table VIII.2

Estimates by an FAO/WHO Committee of the Absorption of Iron from Diets Containing Different Proportions of Foods of Animal Origin[a]

Type of Diet	Assumed Upper Limit of Absorption by Normal Individuals
Less than 10% of Energy from Foods of Animal Origin	10%
10-25% of Energy from Foods of Animal Origin	15%
More than 25% of Energy from Foods of Animal Origin	20%

[a] Reference 4.

Table VIII.3.

A Model of the Utilization of Iron in Pregnancy

Component of Utilization	Amount of Iron (mg)
1. Deposition in Fetus, Placenta, Uterus, Breasts and Increased Haemoglobin Mass	800
2. Loss at the End of Pregnancy in Fetus, Placenta and Blood	550
3. Net Retention after Pregnancy in the Red Cell Mass and Uterine and Breast Tissues	250
4. Basal excretion During Pregnancy	250
Gross Utilization (1 + 4)	1050
Net Utilization (actual cost) (2 + 4)	800

that it receives become very important. The figures in Table VIII.1 are based on the assumption that after 2 months of age a mixture of milk and infant foods is fed and that for this mixture the upper limit of iron absorption is about 15%. For younger infants, breastfeeding is adequate, but for those not breastfed, the same assumptions may be made as for the infant over 2 months. The recommended intake developed in this manner is below the apparent average intake of infants 6-12 months old as recently reported in Canada (Yeung, D.L., personal communication, 1980) but is consistent with the earlier experience if iron used in fortification at that time had limited bioavailability.

Vegetarian Diets

The recommended intakes given in Table VIII.1 are based upon a mixed diet relatively rich in foods from animal sources and generally resembling the average dietaries recorded in Nutrition Canada. For persons consuming vegetarian diets, these recommendations may underestimate the actual needs for iron, particularly if the diet is heavily based upon cereals, but such a situation may be ameliorated if it provides large amounts of ascorbic acid (7).

Pregnancy and Lactation

Several models for the utilization of iron during pregnancy have been constructed (2, 4, 30-34), which in general have drawn upon the same basic data and are in reasonable agreement. The iron actually utilized during pregnancy may be estimated as the summation of the amounts deposited in the fetus, incorporated into haemoglobin in the increased red cell mass of the mother and deposited in tissues involved in pregnancy such as the placenta, uterus and breasts. The total is usually quoted as being about 800-825 mg. Departures from these figures are attributable to different estimates of the desirable increase in red cell mass. Conservative estimates place the figure for the total iron utilization at about 550 mg. To this must be added the continuing basal (urinary, faecal, dermal) losses, which, if taken as 0.9 mg/day (see Table VIII.1), would amount to about 250 mg for the whole pregnancy.

The rate of utilization is not uniform throughout pregnancy. Relatively little other than that to meet basal losses (or to deposit in stores) is utilized during the first trimester. The mother's red cell mass increases sharply during the second trimester and the increase continues at a lower rate into the third. Growth of the fetus is particularly marked in the last part of pregnancy. On a day-by-day basis, peak rates of utilization have been estimated to be of the order of 4 mg/day or higher. If these are to be met directly by the diet, a very major increase in the needs for dietary iron can be predicted. Not all of this iron, however, is lost from the body. The actual losses, or the true cost of

pregnancy, in addition to the basal losses of the mother, consist of the iron contained in the fetus and placenta and in the blood lost at delivery and in subsequent bleeding. Most of the models of iron utilization include a figure of about 500-600 mg as the sum of these losses, but again, opinion is not uniform. The major differences are related to estimates of blood loss at and after delivery, and in the models cited, these represent a variation in losses of iron from 100 to 600 mg. Most of the models provide for a net retention by the mother of about 250 mg of iron at the end of pregnancy, which is in the increased haemoglobin mass and that presumably returns to the body's iron stores.

These estimates may be summarized in a typical model as presented in Table VIII.3.

If the mother has reasonable iron stores before pregnancy, 250 mg may be drawn from them to meet the peak demands of the pregnancy and the net utilization can be considered as the additional amount of iron needed from dietary sources. Conversely, if there are no maternal stores, the full cost of pregnancy would have to be met from dietary sources on a day-by-day basis, and peak rates of utilization would impose a major increase in the dietary requirement. Failure to meet these needs would be reflected in a failure of expansion of the red cell mass with consequent anaemia. It appears that, except in severe anaemia, there is no interference with the deposition of iron in the fetus.

The net cost of pregnancy portrayed above (800 mg) is only slightly above the iron utilization allowed for the menstruating woman ($280 \times 2.62 = 735$ mg). Expressed as an increase in the iron requirement above that allowed for the menstruating woman, the net utilization model would suggest the need for an additional 70 mg of iron (0.25 mg/day) and the gross utilization model would suggest the need for an additional 315 mg (1.13 mg/day). In consideration of the peak daily demands, however, the latter model implies a need for as much as 1.4 mg/day of the additional absorbed iron. If the same efficiency of utilization is assumed for the pregnant as for the menstruating woman, the following total dietary requirement for iron is implied: net utilization model, 15 mg/day; gross utilization model, 20 mg/day; peak utilization prediction, 23 mg/day. As noted earlier, it appears that many, if not most, women entering pregnancy in North America have very low iron stores. On this basis, the higher estimates of dietary iron requirement would hold.

There have been three major studies of iron absorption in pregnancy (35-37). All have demonstrated major increases in the absorption of test doses or of dietary iron during the third trimester, sufficiently high to compensate for the high rates of utilization predicted above without change in the dietary intake; but interpretation of

these findings is difficult. Is increased absorption a physiological adjustment that takes place without serious depletion of maternal iron or is it a consequence of the development of a true iron deficiency that can occur in nonpregnant women? Both interpretations have been applied, with widely different views of the resultant requirement for dietary iron. It is clear also that the usual haematological indices shown by unsupplemented pregnant women can be raised by the provision of additional iron (suggesting, perhaps, that the needs are not being met), but it is not clear that these increases confer any particular physiological benefit to the woman or the fetus.

It is suggested that if iron stores are present before pregnancy, the recommended intake for the pregnant woman should be increased by 1 mg/day over that for the menstruating woman, but if stores are very low or absent at the beginning of pregnancy, it should be increased by 6 mg/day to a total of about 20 mg/day. The latter situation probably holds for many women in Canada at the present time. If so, it is recognized that the increase in the recommended intake may be very difficult to meet by diet alone.

In lactation, iron must be provided to compensate for that secreted in the milk. Reported amounts in mature breast milk range from 0.3 (25, 26) to 1 mg/L or more (27, 28). The lower estimates are more recent and seem to be more appropriate descriptors. The volume of breast milk secreted after about 3 months averages 750 mL/day with a 15% coefficient of variation, so that with an allowance for variation, the iron secreted in it might be 0.3 mg. During early lactation, the concentrations of iron are higher (25, 26) although the volumes of milk are lower, and total secretion might approach 1 mg/day in early lactation. These estimates, with addition of the expected basal iron losses (0.87 mg/day), bring the total need for absorbed iron to 1.17-1.87 mg/day, and if there is 15% absorption, the dietary need would be 8-12 mg/day, a figure below the recommended intake for a menstruating woman. In this calculation it is assumed that menstruation has not been resumed. It has been reported that as many as one-third of lactating primiparae resume menstruation within 3 months (38); but no estimates of menstrual losses by these women are available.

The recommended intake for lactating women is the same as that for menstruating women, 14 mg/day.

Excessive Intakes of Iron

Iron overload, with adverse effects on health, does occur in man. In most cases it is the result of the administration of iron by the intravenous (as in transfusion) or intramuscular route thereby bypassing the normal regulatory mechanisms in the gut mucosa. It has been reported also in situations in which the source of the excess iron

was food but these situations are very unusual in the Canadian context. The most widely described example of such a situation is in the case of South African Bantu men who consume in fermented beverages large amounts of iron that seem to overcome the normal regulatory process; and it is generally thought the high concomitant intake of alcohol is an important contributing factor. A second widely recognized situation of iron overload occurs in idiopathic haemochromatosis, in which the affected individuals absorb excessive amounts from normal diets. It is now thought that this represents a hereditary defect in the process that regulates absorption. Excellent discussions of both of these situations are presented by Bothwell *et al.* (2).

Unfortunately, neither of these situations is of direct relevance to the question of a safe upper limit to iron intake in the Canadian context. Indeed, at present there is no direct information to suggest such a safe level. It is clear that some individuals have taken pharmaceutical supplements that provided quite high intakes, but there has not been a systematic search for and examination of such individuals to see whether there are any signs of latent iron overload. At present it seems very unlikely that iron overload will develop spontaneously from the ingestion of diets rich in iron unless there are genetic abnormalities of disease states that affect its metabolism. Concern about potential overload arises in the connotation only of excessive iron supplementation or possibly major changes in fortification practices.

Acute iron toxicity, with localized gastro-intestinal symptomology as well as systemic effects, has been reported as a result of overdosage with pharmaceutical sources of iron. It has not been reported as a response to any levels of dietary iron.

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Iodine

The adult human body contains 15-20 mg of iodine, of which 70-80% is concentrated in the thyroid gland. Of the other 20-30%, concentrations are highest in the salivary glands, gastric glands and dense connective tissue, and the rest is distributed evenly throughout the body. The total amount of iodine in the thyroid varies with the intake, the age of the individual and the activity of the gland. Iodine in the tissues occurs in both the free inorganic and the organically-bound form, the former at a concentration of less than 0.01 μg/g of tissue. In tissue other than that of the thyroid, the organic form is present mainly as thyroxine, together with small amounts of other compounds such as triiodothyronine. In the thyroid gland, iodine is in the inorganic form and in mono- and diiodothyronine, thyroxine, triiodothyronine, polypeptides containing these iodinated residues and thyroglobulin (1).

The only known function of iodine is its role in the synthesis of the thyroid hormones. These are required for normal calorigenesis, thermoregulation, intermediary metabolism, protein synthesis, reproduction, growth, development, haematopoiesis and neuromuscular function (2). The thyroid takes up iodide by an active transport mechanism that requires energy. The iodide is then oxidized to elemental iodine, combines with tyrosine to form either mono- or diiodotyrosine, which in turn combines to form either thyroxine or triiodothyronine. These are linked by peptide bonds to form thyroglobulin, which contains about 99% of the iodine in the gland and functions as a storage depot for it (1). The hormones are released from the gland by proteolytic breakdown of the thyroglobulin. The normal human thyroid secretes approximately 51.6 μg of iodine in thyroxine

and 11.9 μg in triiodothyronine per day (3). To ensure an adequate supply of hormone, the thyroid must take up 60 μg of iodine per day.

The activity of the thyroid is regulated through a negative feedback mechanism. When the concentration of thyroid hormone drops, the hypothalamus secretes thyrotropin releasing hormone, which in turn stimulates the adenohypophysis to release thyroid stimulating hormone, and this causes the gland to release thyroid hormone and to trap iodine (1). When the average iodine intake drops to below 50 μg/day for a prolonged period of time, the thyroid regulating hormones induce a proliferation of thyroid epithelium that results in goitre. The enlarged thyroid secretes normal amounts of hormone. In cases of severe iodine deficiency, the goitre secretes relatively more triiodothyronine than thyroxine and thus preserves euthyroidism by producing a metabolically more active hormone that contains 25% less iodine (4). A serious consequence of an insufficient intake of iodine during pregnancy is cretinism (5).

Human iodine intakes in excess of 2000 μg/day should be regarded as potentially hazardous. The adverse effects of an increased intake are: temporary increases in the absolute uptake of iodine and its incorporation into organic compounds; inhibition of release of iodine from the thyroid; inhibition of its incorporation into organic compounds and iodine goitre formation; saturation of the active transport mechanism (6). Alternatively, excess iodine can induce hyperthyroidism. This can occur especially in some individuals who have previously had a prolonged deficiency of iodine during which the thyroid functioned autonomously at a hyperactive level but did not manifest hyperthyroidism because of the limitation imposed on hormone synthesis by the low iodine intake (7).

Iodine in food is mainly as inorganic iodide. It is rapidly and completely absorbed in this form at all levels of the gastro-intestinal tract. Newly-absorbed iodide permeates all tissues and rapidly reaches equilibrium in the inorganic iodide pool. In addition to exogenous iodide from the diet, the inorganic iodide pool is continuously being replenished endogenously from the saliva and gastric juices and the breakdown of thyroid hormones. Iodide is continuously lost from the pool by the activities of the thyroid, kidneys, salivary glands and gastric glands. That taken up by the thyroid is incorporated into organic compounds and either stored or released as thyroid hormones. In the circulation, the hormones are bound to thyroxine-binding globulin, to prealbumin and to albumin, with less than 0.07% existing in the free state. Approximately 10% of the thyroxine and 56% of the triiodothyronine are metabolized daily, with 80% of the liberated iodide going back into the pool. The remainder is lost to the body (1).

There is no renal homeostatic mechanism to keep the plasma level of iodine constant (1). When the intake is low, most of the absorbed iodine is utilized by the thyroid, whereas when it is high, the amount exceeding the requirements of the gland is excreted by the kidneys. The normal thyroid continues to produce the amount of hormone required for homeostasis despite a variable intake of iodine. When the intake increases, more iodide is taken up by the gland but without a concomitant change in hormone secretion (2).

Since iodine that is not utilized by the thyroid is excreted by the kidneys, the mean urinary level is a good indicator of the dietary intake. In the adult population, daily excretions of less than 50 but more than 25 μg/g of creatinine are indicative of moderate iodine deficiency, which may lead to the development of endemic goitre in some individuals, especially children and pregnant and lactating women (8). The median urinary excretion levels of iodine recorded in the Nutrition Canada survey ranged from 181 to 440 μg/g of creatinine depending on the age group (9), which indicates that Canadians consume iodine in excess of their physiological needs.

The largest portion of the iodine in the Canadian diet is provided by salt. All of the salt that is sold in Canada for table and general household use must contain 76 μg of iodine per gram (10). Milk and eggs are also major dietary sources (11). Seafoods are exceptionally rich sources but contribute relatively little because they are not a major dietary item (2). The amount of iodine in meat, milk and eggs varies with the amount in the animals' feed (12). Iodine enters the diet also from adventitious sources such as iodophors, used as sanitizers in the dairy industry, iodates, used as dough conditioners, and erythrosine dye (13-15). The average amount of salt consumed by Canadians has been reported to be approximately 10 g per person per day (16). If one-half of this is salt used in the household, this alone would provide 380 μg of iodine per day. A recent survey of samples of milk found iodine levels of 384-511 μg/L (17). A mean intake of 636 mL of milk per day by adolescent males and 432 mL/day by adolescent females was reported in the Nutrition Canada Survey. (9). This would contribute another 300 and 200 μg, respectively, to the daily diet. These are high intakes, but there is no direct evidence that they have any adverse effects. Some foods such as rutabagas, turnips and cabbages contain compounds that have been shown to produce goitre in experimental animals. Human goitre caused solely by dietary goitrogens is probably uncommon in Canada, especially in view of the high intakes of iodine (18).

The assessment of man's requirements for iodine is difficult because of wide individual variation. Dietary intakes of as high as 134 μg/day have been reported for patients with iodine deficiency goitre, and positive iodine balances have been reported in subjects with intakes as

small as 44 μg/day (1, 19). Wayne *et al.* (19) based their calculations of requirements on quantitative studies of iodine metabolism. They calculated that a high normal rate of renal clearance of 55 mL/min and a high normal faecal excretion of 40 μg/day would necessitate an intake of 160 μg/day to maintain the plasma level of inorganic iodide at 0.15 μg of iodine per 100 mL (normal range, 0.08-0.60). Other balance studies have found that intakes ranging from 44 to 162 μg of iodine per day are necessary to maintain positive balance (1). Consequently, the recommended intake for both adolescents and adults is set at 160 μg/day. Mature human milk provides 4-9 μg of iodine per 100 kcal (1-2 μg/100 kJ) and formulae for infant feeding sold in Canada must contain 5 μg/100 kcal (1.2 μg/100 kJ) (10, 20). These amounts appear to be adequate, so that 5 μg/100 kcal per day are recommended for infants. This amount is similar to that recommended for adults when their requirement is related to the requirement for energy. Consequently, the amounts recommended for children are also based on their energy requirements. Lactating women must provide up to 45 μg of iodine per day in their milk; therefore it is recommended that their intake be increased by 50 μg/day. For pregnant women, an additional intake of 25 μg/day is recommended to meet the needs of the growing fetus.

Available data are not adequate to allow the establishment of maximum safe levels of intake of iodine. Intakes of up to 1000 μg/day can be considered safe but 2000 μg/day should be considered toxic, according to one report (2). No adverse effects in people with normal thyroid function have been reported at levels that are at present available in the Canadian food supply.

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Zinc

Zinc is an essential element for plants, animals and man. Zinc metalloenzymes such as carboxypeptidases, dehydrogenases, RNA and DNA polymerases, carbonic anhydrase, alkaline phosphatase, phospholipase C and pyruvate carboxylase, and enzymes dependent upon zinc such as arginase, lecithinase, enolase and deoxythymidine

kinase play important roles in the metabolism of proteins, carbohydrates, lipids and nucleic acids (1-3). In man, symptoms of chronic deficiency of zinc include retardation of growth, hypogonadism, oligospermia and anorexia, whereas hypogeusia, alopecia, diarrhea and dermatitis occur in iatrogenic deficiency (1). In deficiency, the levels of zinc in blood, serum, urine and hair decrease, and the activities of zinc dependent enzymes decrease (1, 2, 4). Zinc deficiency has also been implicated in impaired wound healing, abnormal immune response and in genetic diseases like acrodermatitis enteropathica and sickle cell disease (1).

Retardation of growth and hypogonadism due to zinc deficiency have been reported from Egypt and Iran, attributable in part to the high level of fibre and phytate in the common diet of the affected people (1). Marginal intakes of zinc have been implicated in hypogeusia, anorexia and poor growth in some American infants and children. Cases of deficiency caused by the lack of zinc in preparations for oral and intravenous alimentation have been reported from different parts of the world (1).

The results of chemical analysis of cadavers (5) and of kinetic studies with ^{65}Zn (6) have indicated that the amount of zinc in the human body is 30 mg/kg of lean body mass, thus the body of an adult male is estimated to contain about 2 g of zinc. The highest concentration occurs in the retina and choroid of the eye and in the prostate gland. Zinc in bone is a significant part of the total but it is not easily available to meet the needs of the soft tissues when the intake is inadequate (1).

The mixed Canadian diet provides about 5 mg of zinc per 1000 kcal (6 mg/5000 kJ), about half of which is derived from meat, fish and poultry (7, 8). Red meat, liver, egg yolk, shellfish, poultry, milk, cheese and whole grain cereals are good sources of zinc (9). Mature human milk contains about 0.8 mg/L and colostrum and early milk contain more than 4 mg/L (10, 11). The zinc content of cow's milk is about 4 mg/L (9).

The absorption of dietary zinc depends upon the amount, the source, the presence of certain factors that promote or impair the absorption, and the zinc nutritional status, the age and the physiological state of the subject. Even with an abundant supply of zinc, the concurrent ingestion of phytate, fibre or a high level of phosphate or copper reduces its absorption. Chelating agents such as ethylenediaminetetraacetate in the presence of phytate, some amino acids, *viz.*, histidine, cysteine and methionine, and a high level of dietary protein enhance the absorption of zinc (1, 12, 13). Vitamin C does not affect zinc absorption (14). During late pregnancy and during lactation the absorption of zinc increases in rats (15). With increasing

age in the rat and the calf there is a marked fall in the efficiency of absorption of dietary zinc (16, 17).

The retention of zinc by children 2 years of age was found to be 53% from a diet that provided 4.3 mg/day (13). The results of balance studies on preadolescent girls indicated that the apparent absorption of dietary zinc (without allowance for endogenous faecal zinc) varied from 25 to 62% with an average of 35% (18). When the diet was low in protein or the protein was derived from plant sources, however, the absorption decreased to less than 15%. In three series of balance trials conducted over a period of 15 years, the average apparent absorption of zinc by pre-adolescent children consuming diets that provided 4.6-14.6 mg of zinc per day was 27% (19, 20). In male adults on a meatless diet low in hemicellulose the apparent absorption of zinc was 22% (21). The true absorption of inorganic zinc added to a formula diet consumed by adult females was found to be an average ($\pm$ SD) of 38 $\pm$ 16% (22).

The retention of ^{65}Zn administered orally to fasting human adults varied from 25 to 90% (13). When ^{65}Zn was used as an extrinsic label in white or whole meal bread, the true absorption ranged from 8 to 38% depending on the foods consumed with the bread (23). In view of the results of these recent studies, the true absorption of zinc from the Canadian diet by subjects in different age and sex groups is estimated to be up to 30%.

The average obligatory zinc loss by young women on a formula diet low in zinc (0.17 mg/day) has been reported to be 1.6 mg/day (24). The endogenous faecal and urinary losses were determined by extrapolation to the beginning of the ingestion of the diet. When similar extrapolation was applied to the loss in sweat, the total loss did not exceed 1.8 mg/day. Expressed on the basis of metabolic body size, the daily obligatory loss of zinc was 90 $\mu g/kg^{0.75}$. Since the menstrual loss was negligible (5 μg/day), the obligatory loss by males can be calculated on the same basis. In hot climates the loss of zinc in sweat can be as high as 4 mg/day (12). The urinary excretion of 0.3 mg/day by adult women, reported by others (25), was somewhat less, whereas the loss in sweat by adolescent children, estimated by the arm bag method, was much higher (1.4 mg/day) than the value on which the above calculation of the total obligatory loss is based (20). The lower estimate of zinc loss based on the 24-h collection of sweat from the whole body is considered to be more accurate than that based on the arm bag method.

Although it is known that human growth from infancy to adulthood is not uniform, exact information about the rate of increase in total body zinc is not known. Moreover, the change in the zinc content of various tissues with age follows different patterns (13). On the basis

of the zinc content of a full-term infant at birth (60 mg) and of an adult male and female (2.0 and 1.5 g respectively), the average gain of zinc has been estimated to be 0.2-0.3 mg/day (26). The higher value (0.3 mg/day) was assumed to be the requirement for growth.

Since the total amount of zinc in the newborn infant is about 60 mg (26) and most of the accretion by the fetus occurs in the second and third trimesters of pregnancy, an extra amount of 0.4 mg/day during this period has been allowed for in the requirement for pregnancy. This is in agreement with a recent estimate of a median additional zinc requirement of 0.21-0.68 mg/day during the third trimester (27). In lactation, the initial concentration of zinc in the milk is about 1.6 mg/L. It falls to about 1 mg/L by 3 months and to about 0.8 mg/L after 6 months (11, 28, 29). On the assumption that there is a concentration of 1.2 mg/L and a mean output of 750 ml of milk per day, the average secretion in the first 3 months would be 1.6 mg/day. With allowance for variability, this would become 2.1 mg/day.

Recommendations

The recommended intakes of zinc from the age of 13 are 9 and 8 mg/day for males and females respectively. They are based on daily obligatory losses of 90 $\mu g/kg^{0.75}$, a growth requirement of 0.3 mg, a factor of 1.3 for individual variability and a 30% true absorption. The recommended intake of 2 mg/day for young infants is based on the observed intakes at the breast for up to 3 months. Since the zinc in human milk is better utilized than that in cow's milk (30, 31) infants fed formula may require larger amounts. From 3 months to 12 years, efficiency of absorption is assumed to be the same as for other age groups, and the recommended intakes increase from 3 to 7 mg/day.

The recommended intake of 6 mg/day for children 7-9 years old is in agreement with the results of balance studies, including losses in sweat, in preadolescent girls (20). The recommended amount for adult males compares favourably with the estimate of requirements based on the regression analysis of data from balance studies in which loss in sweat was not included (32).

Among dietary trace elements, zinc is relatively non-toxic. Pharmacological doses of 150 mg/day in zinc sulphate have been given orally for almost a year with no adverse effects, but patients receiving such a dose of zinc for a longer period may suffer from copper deficiency because of the well-known antagonism between zinc and copper (1, 33). The ingestion of massive amounts of zinc over short periods of time causes abdominal pain, nausea, vomiting, dehydration, electrolyte imbalance, lethargy, dizziness and muscular incoordination (1).

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Copper

As a component of many metalloenzymes, copper plays a vital role in mammalian metabolism. It forms part of the molecular structure of cytochrome *c* oxidase, copper amine oxidases, superoxide dismutase, ascorbic acid oxidase, tyrosinase and ferroxidase, including ceruloplasmin (1). There is also a copper binding protein of low molecular weight in liver and intestinal epithelium that probably detoxifies copper in the liver and controls its passage through the intestinal cells (2).

Manifestations of a deficiency of copper in animals include anaemia, cardiovascular lesions, skeletal deformities, demyelination and degeneration of components of the central nervous system, reproductive failure and imperfect keratinization and pigmentation of hair and wool (1). Deficiency of copper is rare in man but it has appeared in malnourished infants, including some with chronic malabsorption, and premature infants fed milk formulae low in copper. It has also been seen in patients who received prolonged total parenteral nutrition and in cases of hypoproteinaemia with accompanying losses of copper through the gastrointestinal or urinary tract (3). Indicators of copper deficiency in man are leukopenia, persistent neutropenia, varying degrees of anaemia and, in infants, skeletal demineralization (3).

Copper is widely distributed in foods, shellfish, nuts, liver, kidney, dried legumes and whole grain cereals being among the best sources. The concentration of copper in drinking water depends upon the hardness of the water (from less than 50 μg/L in hard water to more than 500 μg/L in soft water carried in water pipes (4)).

Requirements

Children and Adults

Analyses of self-chosen and hospital diets in Canada, the United States, New Zealand and Finland have revealed daily intakes of copper of up to 3.48 mg (5-7) but in most cases they were less than 2 mg. These amounts are considerably lower than earlier estimates of 2-5 mg/day, which may be the result of changes in methods of food processing or improvements in analytical techniques. Balance studies have been used to estimate the dietary copper requirements of man but they cannot be used to determine how much is truly absorbed because the faeces contain both unabsorbed and biliary copper (8). Balance studies on preadolescent girls in the United States, who ate mixed diets, showed negative copper balances with intakes of 1.0-1.3 mg/day (35 μg/kg of body weight per day) (9) but intakes of 1.6-2.1 mg/day have been shown to produce equilibrium or slight positive balance in pre-adolescent American girls (10) and women in New Zealand (11).

In contrast to these, Taper *et al.* (12), who did not take into account losses in sweat and through the skin, reported that a copper intake of 2 mg/day was not sufficient to maintain balance in young adult women in the United States. From the most recent metabolic study on healthy American men, Klevay *et al.* (13) calculated that an average requirement was 1.55 mg/day, which included an allowance of 0.25 mg to compensate for losses from the surface of the body. This is comparable with estimates of 1.67 (14) and 1.25 mg/day (15) that were made several years earlier. The copper requirements of patients on total parenteral nutrition have been reported to be 300-500 μg/day (16). Discrepancies in the levels of intake that have been reported as necessary to maintain equilibrium may have arisen from the short duration of the studies and/or the lack of precise information on copper intakes of subjects before the studies were made.

From present knowledge, it is not possible to make satisfactory estimates of requirements for and recommended intakes of copper but there is support for the statement that dietary intakes of 2 mg/day are above the actual needs of children and adults. This amount is close to that provided by the average Canadian diet and there is no evidence that the general population is at risk of copper deficiency.

Infants

The concentration of copper in cow's milk is very low. In human milk it varies with the stage of lactation, being highest at the beginning, about 0.6 mg/L, then decreasing to about 0.2 mg/L (17,18). Infants fed exclusively from the breast receive 40-60 μg of copper per kilogram of body weight per day at 3 months of age (17,19), and when mixed feeding has begun, an infant 6 months of age receives approximately

70 μg/kg per day (20, and MacDonald, L., personal communication).

In a neonate at normal term, the concentration of copper in the body is about three times that in an adult, and reserves in the liver are usually sufficient for the first 4 months of life even if the dietary intake is minimal (1). The levels of copper in most tissues decrease during the first year, with a corresponding increase in the concentrations of ceruloplasmin and copper in plasma (21) and copper in hair (22). Several estimates of the copper requirements of infants have been made, which generally give figures between 50 and 100 μg/kg of body weight per day (23), but there is one that gives a total of 200-500 μg/day from a study that showed that children with intakes as low as 35 μg/kg per day were in positive balance (24). Most manufacturers of food formulae for infants now include copper at about 60 μg/100 kcal (15 μg/100 kJ), the level recommended for formulae for full-term infants by the Committee on Nutrition of the American Academy of Pediatrics (25).

It is apparent that satisfactory estimates of requirements for and adequate intakes of copper for the infant cannot be made, but the information outlined above indicates that a dietary intake of 80 μg/kg of body weight per day is safe and probably above actual requirements.

Toxicity

Chronic or acute toxicity from copper is rarely encountered, although there is one report that a high level in drinking water may have caused copper poisoning in an infant 15 months of age (26). An FAO/WHO report (27) suggests that if the copper intake of man does not exceed 0.5 mg/kg of body weight per day, no deleterious effects are to be expected.

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Fluoride

Fluoride occurs mainly in the bones and teeth where its concentration increases with age at a rate that is strongly influenced by the amount in the water supply. Where the water naturally contains 1.0-1.2 parts per million (ppm (mg/kg)) of fluoride, the concentration in the enamel and dentin of the teeth of the people is approximately 50% greater than it is where the water supply contains 0.3 ppm or less (1). The higher concentration is associated with a marked decrease in the incidence of dental caries in children. Addition of fluoride to the drinking water to bring the concentration to 1 ppm results in a reduction in tooth decay of at least 50% during childhood (2). Fluoridation of urban water supplies that are low in fluoride is the most effective public health measure for the prevention of dental caries.

Water supplies that naturally contain an unusually high concentration of fluoride, 2 ppm or more, induce a mottling and discolouration of tooth enamel (chronic endemic dental fluorosis) (3). There are no other known adverse effects of the consumption of water that naturally contains moderately high levels of fluoride, and indeed, it has been suggested that a fluoride concentration of 4 ppm or more may

provide protection against osteoporosis in older adults (4). Fluoridation of water to a level of 1 ppm appears to have no effect on susceptibility to osteoporotic bone disease (5, 6).

Most of the foods that are consumed in North America contain 0.2-0.5 ppm of fluoride on the basis of dry matter. The concentrations in seafoods, however, range from 5 to 15 ppm and a cup (about 235 mL) of tea contains 0.1-0.2 mg. Cooking foods in fluoridated water significantly increases their fluoride content.

The total intake of fluoride by adults living in a Canadian community with a fluoridated water supply has been estimated to be 2-5 mg/day (7). The average daily intake of fluoride in foods consumed by urban populations in the United States has been estimated at 2.6 mg in fluoridated regions and 1.0 mg in non-fluoridated regions (8). The fluoride intakes from both food and water ranged from approximately 1 mg/day in low fluoride regions to 4 mg/day in those with a fluoridated water supply. Fluoridation has been reported to have no effect on the fluoride content of breast milk, which has been found to average 0.05 ppm (9).

The intake of fluoride may be significantly influenced by factors other than fluoridation of water, including the season of the year (which influences water consumption), food fortification practices and cultural food habits. The average fluoride intake of adults in Newfoundland has been estimated at 2.7 mg/day despite a water supply low in fluoride (10). This circumstance may be attributed to the addition of bone meal to flour in that province and also an unusually high consumption of tea.

About 80% of ingested fluoride is absorbed, the efficiency of absorption being somewhat greater from water than from food. Concentrations of fluoride in the blood are kept within narrow limits by an efficient mechanism of renal excretion (11). Impaired kidney function results in the accumulation of fluoride in bone. Under conditions of heavy sweating, nearly 50% of the total fluoride excreted may be in the sweat. There is limited transfer of fluoride across the placenta (11).

Whether fluoride has a biological function other than the formation of fluoroapatite in bones and teeth is controversial. Earlier evidence that it is required for reproduction and the prevention of anaemia in mice has been discounted by the results of a more recent study (12). An increase in growth and pigmentation of incisor enamel in response to 2.5 ppm in the diet has been reported in rats kept in a very clean environment and previously fed a highly purified diet containing less than 0.5 ppm of fluoride (13). Fluoride also has been reported to protect against nephrocalcinosis in growing rats (14). In any event, the prevention of dental caries in children, with benefits

that extend to adults, is an adequate basis for classifying fluorine as an element essential for human health.

An excessive absorption of fluoride, usually associated with a chronic exposure to it in an industrial setting or sometimes an excessive dietary intake, is associated with an abnormal condition in bone called fluorosis. Some changes have been seen by radiographic examination of adults exposed throughout life to a water supply containing about 8 ppm of fluoride, but these changes produced no symptoms (3).

It is generally accepted that near maximum dental benefits are conveyed at concentrations of 0.7-1.0 ppm in drinking water in temperate climates, and that adverse changes in tooth or bone are not produced at those levels.

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Manganese

A normal man who weighs 70 kg contains 12-20 mg of manganese distributed throughout the body, the highest concentrations being in tissues with a high content of mitochondria (1). Manganese can function as a cofactor for literally hundreds of enzymes but in most systems it can be replaced by other metals. It is the most efficient cofactor in the synthesis of chondroitin sulphate, and some of the symptoms of manganese deficiency in animals are linked to a deficiency in the formation of mucopolysaccharide (2). Manganese is bound to RNA, where it presumably functions to maintain the native structure, and it may also be necessary for RNA polymerase activity (3). It may therefore be intimately involved in the synthesis of nucleic acids and proteins. It is also a constituent of a superoxide dismutase enzyme.

Manganese is equally well absorbed throughout the length of the small intestine but iron and cobalt may compete with it for absorption (1). Its rate of absorption is proportional to its concentration in the lumen of the intestine. Subsequent to absorption, Mn^{2+} is oxidized to Mn^{3+}, which then forms a complex with a plasma protein, transmangin (4). The homeostatic control of manganese depends upon efficient excretion, primarily in the bile, rather than upon selective absorption. Secondary routes of excretion are in the pancreatic juices and passage across the mucosa back into the intestinal lumen. These routes are interdependent and interact to maintain homeostasis. If the biliary route is overloaded, excretion via the pancreas increases. Very little manganese is excreted in the urine, even when it is injected parenterally (1, 4).

Deficiency of manganese in species other than man has severe and sometimes irreversible effects, such as failure of growth, skeletal abnormalities, depressed reproductive function and, in the newborn, ataxia (4). Only a single case of human manganese deficiency, in a

patient inadvertently given a purified diet that did not include it, has been observed to date. This patient showed loss of weight, transient dermatitis, occasional nausea and vomiting and reddening of the colour and slowing of the growth of the hair and beard. He had a marked hypocholesterolaemia and a prolonged blood clotting time that could not be rectified by treatment with vitamin K unless manganese was also given. It was postulated that manganese is required for the biosynthesis of glycoproteins involved in the blood clotting process and that it is a cofactor in the biosynthesis of cholesterol (5). Under normal circumstances, however, an adequate intake and efficient homeostatic control effectively combine to prevent manganese deficiency in man (3).

Manganese is one of the least toxic elements for man. Although chronic poisoning from it may occur as a result of contamination in an industrial setting, no case of toxicity in man arising from excessive dietary intake has ever been reported (1).

Several Canadian studies, the results of which were made available between 1972 and 1981, suggest that average intakes of manganese are 2.0-4.1 mg/day (6-9), provided primarily by grains, leaves and fruit (4, 10).

At present there is insufficient information from studies on dietary intakes and metabolic balance from which to derive satisfactory estimates of dietary requirements of manganese. Balance studies on normal subjects ingesting a wide variety of foods have shown that intakes from 2.47 to 10.70 mg/day all resulted in positive balances, whereas an intake of 0.71 mg/day resulted in negative balance (10). Consequently, it seems clear that for adults and adolescents 2.5 mg of manganese per day is above the actual need and lower intakes may be adequate. During the first, second and third months of life, infants fed exclusively from the breast receive only 0.9, 0.6 and 0.5 μg of manganese per kilogram of body weight per day, respectively (11). In a study made in Canada, infants fed a combination of breast milk and formula received 12, 27 and 71 μg/kg per day at 1, 3 and 6 months of age (12). As is the case with adults, however, there is insufficient information on which to base specific recommendations for infants and children. The Canadian Food and Drug Regulations (13) requires a minimum of 5 μg of manganese per 100 kcal (12 μg/1000 kJ) in formulae for infant feeding. This is the same amount recommended by the Committee on Nutrition of the American Academy of Pediatrics (14). In girls 6-10 years old, 45 μg/kg per day has been shown to be sufficient to maintain balance, although much less may be required (15). Since the developing fetus demands very small amounts of manganese, and the levels in human milk are less than 6 μg/L, pregnant and lactating

women need not increase their intakes over those normally consumed by adults.

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Selenium

Although the essentiality of selenium for domestic and laboratory animals has been recognized for some years, it is only recently that direct evidence for a human requirement and substantial information about the selenium content of human diets have become available.

Selenium decreases or replaces the requirement for vitamin E in the prevention of several diseases of domestic animals, including myopathies in calves and lambs, exudative diathesis in chicks and liver necrosis in swine. It has been shown that in many cases these diseases are associated with a low level of selenium in soils and feedstuffs along with an inadequate intake of vitamin E. Diets deficient in selenium but with adequate vitamin E lead to deficiency syndromes marked by pancreatic fibrosis in chicks (1) and by depression of growth, reproductive failure and hairlessness in rats (2).

The nutritional interrelationship between selenium and vitamin E stems from a mutual involvement in the metabolism of peroxides and of free radicals produced by the oxidation of lipid. Vitamin E probably inhibits the formation of peroxides by acting as a scavenger of those free radicals. Selenium is a constituent of glutathione peroxidase, an enzyme that protects cell membranes from oxidative damage by catalyzing the reduction of hydrogen peroxide and organic peroxides (3). This enzyme contains four atoms of selenium per molecule in selenocysteine. It reduces a wide variety of peroxides but requires reduced glutathione specifically as the reductant. The concentration of the enzyme in tissues is markedly decreased in animals deficient in selenium, and its activity in erythrocytes is an indicator of chronic selenium status (4). The level of selenium in the plasma is a reflection of the short-term intake.

Other selenoproteins have been detected in the muscle, testis, spermatozoa and blood of animals. Their physiological significance is unknown but they indicate that selenium may have other metabolic roles (5).

The presence of glutathione peroxidase in human tissues indicates that there is a dietary requirement for selenium. Although there is no clear evidence of deficiency among people who consume varied diets, a fatal cardiomyopathy designated Keshan disease has been reported to occur among children in some parts of south China who eat a rice

diet very low in selenium (6). Its incidence is markedly reduced when the diet is supplemented with sodium selenite. A syndrome responsive to selenium that is characterized by muscular pain and weakness has been reported in an individual on intravenous alimentation with a formula low in selenium over long periods (7).

The selenium content of Canadian foods is highly variable, partly because of regional differences in the selenium content of the soil (8, 9). In general, grains grown in the prairie provinces are higher in selenium than those grown in the eastern provinces. Some plants, including wheat, accumulate selenium and the content of the grain reflects that of the soil. In four composite diets compounded from foods purchased in three Canadian cities, cereals were found to contribute most of the selenium, followed by meat, poultry and fish (9). Fruits and vegetables are low in selenium. In cereals it is present mainly in selenomethionine and selenocystine.

From food disappearance data, the average intake of selenium in Canada has been estimated to be about 200 μg/day (9). Individual intakes vary widely, however, and some diets may contain only half this amount. On the basis of dry weight, four composite diets were found to contain 0.15-0.30 μg/g (9). A typical Canadian diet comprised of 11 food groups has been estimated to provide 170 μg of selenium per day. A concentration of 0.1 μg/g of diet, on a dry weight basis, meets the selenium requirement of several mammalian species (10,11). The same concentration in an average diet for human adults would provide about 50 μg/day.

The diets of adults residing in some regions of New Zealand and Finland, where the selenium content of the soil and of the food supply is exceptionally low, may provide as little as 25 μg/day (12,13). Such intakes are reflected in low concentrations of selenium in plasma and low glutathione peroxidase activity in erythrocytes (12,13). The selenium intake of infants in these regions is about 5 μg/day. No pathological symptoms were found in these subjects, and it was concluded that 20-30 μg/day is adequate for the health of adults (12,13). The results of a recent balance study on male adults in the United States, however, showed that an intake of 70 μg/day was required to maintain their usual plasma levels and body stores (14). These findings suggest that humans may be adaptable to a considerable range of intakes of selenium.

From a knowledge of the known requirements of animals and the intakes of humans, an amount of about 50 μg/day, essentially a median between those two levels, appears to be adequate for adults, and it is readily available from the mixed diets of Canadians. The requirements of other age groups are probably proportional to the total food intake.

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Chromium

Trivalent chromium is required for normal glucose metabolism in experimental animals, probably by acting as a cofactor of insulin (1). Deficiency of chromium has been described in a patient fed parenterally over a long period (2).

At present there is insufficient information on which to base a factorial approach to the estimation of nutritional requirements for chromium. Most of the chromium that is lost from the body is excreted in the urine, but there is insufficient knowledge to allow a satisfactory assessment of the amount. With the use of stable isotope dilution, a range of 0.4-1.8 μg and an average of 0.8 μg/day have been measured (3, 4). A more recent report on the urinary excretion of chromium by healthy young men as measured by atomic absorption spectrophotometry gave an average of 4.3 μg/day (5), which agrees with some earlier reports (6, 7). A satisfactory analytical method is necessary before useful estimates can be made; but even if the urinary excretion of chromium by individuals on a normal diet could be defined, it would be necessary to measure the obligatory loss before a factorial approach to the estimation of requirements could be made. Furthermore, there is no information on the extent of absorption of organically bound chromium, as it occurs in food. Absorption from $CrCl_3 \cdot 6H_2O$ appears to be only 0.5-0.7%, but this may be an underestimate (1).

The intake of chromium by adults on typical western diets is estimated to be 50-100 μg/day (8, 9). Average intakes of Canadian infants 3 and 34 months of age are 30 and 60 μg/day respectively (10), which appear to be adequate because there is no evidence of deficiency of the type shown when diets that contain no chromium are eaten (2). Although the nutritional status with regard to chromium may be involved in the pathogenesis of diabetes mellitus, it is not known whether this is because of inadequate dietary intake or functional deficiency in cells and tissues (5).

The present state of knowledge supports the opinion that the usual dietary intakes of chromium in Canada fall within a safe range; but it is not possible to estimate requirements.

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Other Trace Elements

The results of experiments with animals have indicated that several trace elements besides zinc, copper, iron, manganese, selenium and chromium are essential for normal growth, reproduction and other bodily functions. These include cobalt, molybdenum, tin, vanadium, silicon and nickel. Deficiencies of these elements have been produced in animals with the use of highly purified diets containing amino acids in place of protein, ultra-clean isolators and in some cases a rigid weaning routine, which prevents accumulation in the experimental animal of the trace element under investigation (1, 2).

The significance of cobalt in the nutrition of man and other non-ruminants is confined to its presence in vitamin B_{12}. Ruminants fed diets deficient in cobalt show gradual loss of appetite, wasting and

anaemia followed ultimately by death (2). Athough molybdenum deficiency in animals has been known for a long time to cause a decrease in enzyme systems that contain it, *viz.*, xanthine oxidase, aldehyde oxidase and sulphite oxidase (2), a combined deficiency of xanthine oxidase and sulphite oxidase has recently been reported in a severely retarded young girl (3). Lack of molybdenum in total parenteral nutrition of a man was also recently implicated in intolerance to amino acids, particularly methionine. Treatment with ammonium molybdate (300 μg/day) improved the clinical condition and reversed the defect in sulphur metabolism (4). Deficiencies of tin, vanadium, silicon and nickel in humans have not been reported but they are essential for the growth of rats, chicks and pigs and for the normal metabolism of bone and connective tissue. Deficiency of nickel or vanadium causes impaired reproduction in animals (2, 5-7).

The intake of nickel by Canadians consuming a mixed diet has been estimated at 350-580 μg/day (8) and that of infants, except those under 1 month of age, has also been found to be within that range when expressed on the basis of the energy intake (9). About half of that amount has been reported in selected diets in the United States (10), although similar amounts have been reported to occur in western mixed diets generally (2). Information on the amounts of molybdenum, tin and vanadium in Canadian diets is not available, but daily intakes of molybdenum of 120-240 μg (11), tin 100-1400 μg (2, 12), silicon 1-1.4 g (2) and of vanadium 10-30 μg (10,12) in western diets have been reported. According to recent findings, the amounts of vanadium in mixed diets are much less than those reported earlier, which is attributed to improvement in analytical methods (13). Cow's milk contains, in microgram per millilitre, molybdenum 0.07, nickel 0.03, vanadium 0.0001 and tin 0.15 (12,13). Because symptoms attributable to frank deficiency of any of these trace elements have not been observed in humans under normal dietary conditions, intakes of approximately those amounts cited above are presumed to be adequate. Nevertheless, epidemiological findings and the results of animal experiments have led to suggestions that inadequate or excessive intakes of trace elements such as chromium, zinc, copper, manganese, vanadium and nickel or imbalance among them may be related to chronic diseases such as diabetes, atherosclerosis and cardiovascular disease (14,15).

Toxic effects of excessive dietary intakes of nickel, vanadium, silicon and tin in man have not been reported. A high incidence of gout in man is associated with molybdenum intakes of 10-15 mg/day in some parts of the Soviet Union. Cobalt intakes as high as 8 mg/day from beer have been implicated as a factor in cardiomyopathy in

Canada and the United States. Respiratory tract neoplasia and dermatitis occur in some workers in nickel refineries, and some miners develop silicosis because of inhalation of silica particles. Toxic levels of these elements, as determined by adding inorganic or organic sources of them to the diets of animals, are much higher than the amounts in human diets. Thus there is a considerable margin of safety (2).

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IX. WATER AND ELECTROLYTES

Water

Water is an essential nutrient, in the absence of which, life as we know it would be inconceivable. It is the vehicle of transport for nutrients and metabolites throughout the body. Practically all metabolic reactions occur in the aqueous medium, and in hydrolytic and hydration reactions water is an active participant. Water is also responsible for temperature regulation through heat loss by evaporation from lungs and skin, and it functions as a lubricant in joints, a cushion for the nervous system and a transport medium for sound in the ear (1).

Water contributes about 75% to the body weight of a newborn infant, 60% to that of a growing child and 50% to that of an adult. The proportion is somewhat lower in women than in men because of their higher body fat content. A little more than half of the body water is intracellular (1).

The intake of water is regulated mainly by thirst but social custom and habit are also significant factors. The average water usage in the adult body, including fluids drunk (1200 mL), moisture ingested in solids (1000 mL) and water of oxidation (300 mL) amounts approximately to 2.5 L/day in a temperate environment, but there are large variations in the amount depending on physical activity and the temperature and humidity of the environment. The daily output of water, comprising urinary (1300 mL) and faecal (60 mL) excretions, evaporative loss through the lungs (400 mL) and sweat loss (800 mL), normally balances the intake. The urinary output is controlled by a nerve centre in the hypothalamus, the antidiuretic hormone secreted by the posterior pituitary and the solute excreted by the kidneys. In hot weather or during heavy physical activity, the water requirement increases by several litres a day to compensate for increased sweating and evaporation through the lungs (2). Prevention or severe restriction of fluid intake by athletes before or during prolonged activity therefore may be harmful (3). The normal intake of water in infancy is greatly in excess of the amount required for growth and for compensation for obligatory losses, and the excess is eliminated partially by evaporation through

the lungs. Infants and young children are, however, susceptible to dehydration due to diarrhea and vomiting because their normal amount of body water is higher and its turnover is faster than in older persons (4).

The requirements for water have generally been estimated to be 1 L/1000 kcal (1.2 L/5000 kJ) of food intake (4). Since the insensible, urinary and faecal losses of water by infants are relatively higher, their requirements are about 1.5 times that amount (5). It should be noted, however, that breast-fed infants do not need additional water (6).

When the loss of fluid exceeds the intake, a dehydration syndrome is induced, which is characterized by a loss of appetite and an impaired capacity for work. With increasing dehydration, heat exhaustion and hallucinations occur and when 10% of the body water is lost, heat stroke results (3). Excessive loss of fluid through perspiration is accompanied by a loss of sodium. If the fluid lost is replaced by water, a condition known as water intoxication results, which is characterized by a drop in blood pressure and weakness. To protect against this, people who work in a hot environment should take approximately 1 g of additional sodium for every litre of sweat lost above 4 L (7).

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Sodium, Potassium and Chloride

Potassium, the major intracellular cation, and sodium and chloride, the predominant extracellular electrolytes, are among the essential factors that maintain acid-base balance and osmotic equilibrium in the body. Serum levels, expressed in milliequivalents (mEq) per litre, are regulated at about 142 for Na^+, 4 for K^+ and 104 for Cl^- (1 mEq = 23, 39 and 35 mg of sodium, potassium and chloride, respectively), by mineralocorticoids and by the intake of water, which is controlled by the thirst centre in the hypothalamus. Movements of sodium and potassium across cell membranes are involved in nerve conduction and muscle action. Deficiency of electrolytes is ordinarily caused by excessive losses from vomiting, diarrhea or sweating, or occasionally by an insufficient intake or an imbalance between the two cations. Symptoms of deficiency of sodium are muscular cramps, mental apathy, anorexia and even coma; whereas deficiency of chloride leads to metabolic alkalosis. Deficiency of potassium is manifested by muscular weakness, cardiac arrhythmias and mental confusion (1, 2).

At birth an infant contains about 80 mEq (1.8 g) of sodium, 50 mEq (2 g) of potassium and 50 mEq (1.8 g) of chloride per kilogram of fat free body tissue, and the concentration of only the potassium increases, to approximately 70 mEq (2.7 g) per kilogram of fat-free weight in the adult (3). The results of experiments in which whole body counters were used have indicated that the bodies of both male and female athletes contain about 70 mEq (2.7 g) of potassium per kilogram of fat free weight but that sedentary males have 10% less and sedentary females have less than the males. The total body potassium of both men and women decreases with age after 50 years (4, 5). The sodium and chloride content of adult males and females, determined by total body neutron activation analysis, has been found to be 25-30% less than the above values (6), which were obtained by the chemical analysis of cadavers. The proportion of the total body sodium in bone is approximately 40% but that of potassium and chloride is very low. Whereas all of the potassium and chloride in the body is exchangeable, the proportion of exchangeable sodium is about 75% (7). The average biological half-life of sodium in the body has been reported to be 9.3 days (8).

The electrolytes are widely distributed in human foods of both plant and animal origin, and a deficiency of any of them under ordinary conditions is unknown. A composite diet (2400 kcal (10 000 KJ)) based on Nutrition Canada, Food Consumption Patterns Report (9) contains 2.8 g of sodium (7 g of salt) and 2.9 g of potassium. Salt was not added in cooking the foods. More than one-third of the salt in the mixed Canadian diet is in commercially processed foods. Information

on urinary excretion by about 400 men and women was in general agreement with the results of the analysis of the diets (10). Deficiency of chloride in infants fed a soy formula low in chloride has been reported to be the cause of retardation of growth and delayed neurological development (11, 12). Human milk contains, in milligrams per litre, 160 of sodium, 500 of potassium and 390 of chloride; and the corresponding levels in cow's milk are 500, 1370 and 1020 (13). Dietary electrolytes are almost completely absorbed. Their excretion in urine is regulated by adrenal cortical hormones, the filtered load of sodium and chloride and the presence of an osmotic diuretic such as glucose in the urine (7).

Requirement and Recommended Intakes

Nutritional requirements for electrolytes have not been well defined but they can be estimated from the limited information that is available on the obligatory or minimal losses from the body, the amounts (based on body composition) required for fetal development and for growth and the amounts secreted in milk during lactation. Obligatory renal losses of each of the electrolytes by adults are about 10 mEq (230 mg of sodium, 390 mg of potassium, 350 mg of chloride) per day. The faecal loss of potassium is approximately 15 mEq (585 mg) per day, and normal faecal losses of sodium and chloride are minimal (14, 15). The loss of sodium in sweat by adults on a low intake of salt is about 5 mEq (115 mg) per day (16). The loss of chloride would be equivalent to that of sodium, since their concentrations in sweat are about the same (16). Information on the loss of potassium in sweat when the intake is low is not available but it can be estimated from the potassium concentration (5 mEq (195 mg) per litre) and the daily volume (800 ml) of sweat from a person in a temperate climate to be less than 4 mEq (156 mg) per day (17). Thus the total minimal losses of electrolytes by adults are approximately, in milliequivalents per day, sodium 15 (350 mg), potassium 30 (1.2 g) and chloride 15 (525 mg); or in milliequivalents per kilogram of body weight per day, respectively 0.25 (6 mg), 0.5 (20 mg) and 0.25 (9 mg). Based upon these amounts, with additions for a margin of safety and individual variation, the recommended intakes for adults are, in milliequivalents per kilogram per day, sodium 0.4 (9 mg), potassium 0.75 (30 mg), and chloride 0.4 (14 mg). When there is heavy sweat loss (> 4 L), an extra intake of about 1 g of sodium (2.5 g of salt) per litre of drinking water is required (2).

In consideration of the body composition of a newborn baby and of an adult, the daily requirements for growth to maturity at 18 years of age are estimated to be less than 1 mEq (23, 39 and 35 mg of sodium, potassium and chloride respectively) of each of the electrolytes per day (3). When adjustment for the amounts retained is made, 1 mEq may be

adequate. Thus intakes, in milliequivalents per kilogram of body weight per day, of sodium 1.4 (35 mg), potassium 1.75 (70 mg) and chloride 1.4 (50 mg) should be sufficient for growth and maintenance up to adulthood.

During pregnancy the total amount of sodium retained is about 900 mEq (21 g). In consideration of the composition of the body and of the accretion of fluids during pregnancy, the amount of potassium retained is estimated to be of the same magnitude as that of sodium, and the retention of chloride may be somewhat less (18). Thus the daily requirements for each of these three electrolytes above the maintenance requirements during pregnancy are calculated to be 3 mEq (69, 117 and 105 mg of sodium, potassium and chloride respectively).

During lactation 5-10 mEq of sodium, potassium and chloride are secreted in 750 mL of milk (in calculations, an amount of 10 mEq is used for all). On the assumption that 30% of the amount in the diet is retained to meet the needs of pregnancy and lactation (19), the additional intakes per day should be 10 mEq of each (230 mg of sodium, 390 mg of potassium and 350 mg of chloride) during pregnancy and 33 mEq of each (0.76 g of sodium, 1.29 g of potassium and 1.16 g of chloride) during lactation. Thus the total recommended dietary intakes during pregnancy are, in millequivalents per day, sodium 25 (0.6 g), potassium 40 (1.6 g) and chloride 25 (0.9 g), and during lactation, sodium 50 (1.2 g), potassium 65 (2.6 g) and chloride 50 (1.8 g).

Intakes

Intakes of sodium chloride from practical customary diets supply much higher amounts of the two electrolytes than those recommended, but under normal conditions the kidneys can make a physiological adjustment (1).

On the basis of the results of experiments on animals, epidemiological observations in different countries and some recent findings of abnormalities in the sodium metabolism of people susceptible to hypertension, it has been postulated that the prevailing high intake of salt in many parts of the world is partly responsible for the high prevalence of hypertension (20). Nutrition Recommendations for Canadians (21) therefore include a suggestion to minimize the consumption of salt. Toxicity due to excessive intake of electrolytes in the diet is not possible, but hypernatraemia, hyperkalaemia and hyperchloraemia can occur under various clinical conditions, with adverse effects on the renal and cardiovascular systems (7). Fatalities have occurred in hospital nurseries when salt has been accidentally used instead of sugar in the preparation of formula or when sodium chloride used as an emetic has not been vomited back (22). A very small proportion of patients receiving enteric-coated tablets containing po-

tassium chloride has been reported to suffer from ulcers and stenosis of the intestine. The excessive ingestion of potassium chloride causes nausea and vomiting so that fatalities even due to an accidental overdose have not been reported (22).

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X. SUMMARY

Recommended Nutrient Intake

A recommended nutrient intake is an estimate of an amount to cover the requirements of essentially all people in a group with similar specified characteristics (age, sex, type of diet etc.). It is conceived as an average requirement plus 2 standard deviations (SD) (see Figure I.1). In most cases a coefficient of variability of 15% is applied, which is equivalent to 30% for 2 SD, because that is the variability widely shown in quantitative biology. It is assumed that except for specified physiological changes such as puberty and pregnancy, requirements change progressively with age during growth, and in such cases the recommended intakes refer to the mid-points of the arbitrarily chosen age groups. The recommended intakes are for healthy people who eat a variety of common foods available in Canada. They are expressed as intakes per day, but they are not recommended as specific intakes for every day but as average amounts per day to be obtained over periods of days or weeks.

Energy

The figures for energy are estimates of average requirements based upon the pattern of activity considered typical of each age and sex group. They are expressed as averages because there is a risk to health from both inadequate and excessive intakes. Individual intakes should be based upon the physical activity and the history of the energy intake in relation to body weight. (See Figure I.1. and Table II.1.)

Carbohydrate and Fibre

There is not adequate knowledge upon which to base estimates of requirements for the proportion of food energy to be provided by carbohydrate and to judge the possible benefits of considerable amounts of fibre in the diet. For guidance, it is suggested that 50% of the food energy should be derived from the available carbohydrate in foods with a high content of complex carbohydrates and fibre.

Fat and Essential Fatty Acids

Fat and essential fatty acids (EFA) are considered in terms of their contribution to the intake of energy. It is recommended that for all age

groups at least 15% of the food energy be provided by fat and that for children and adults 3% of the energy be provided by EFA. EFA are the source of about 5% of the energy value of human milk but of much less in cow's milk. Recommended intakes of EFA are predominantly for linoleic acid.

Protein

Protein is considered in terms of a mixture of proteins of the same quality as that in the average Canadian diet (see Table V.1). The recommended amounts for the population beyond infancy are below the dietary intakes of most Canadians. They are conceived as intakes at which there is a low risk of inadequacy (to maintain nitrogen balance or provide for expected accretion) when the supply of energy is adequate. The recommended intakes for infants are based upon the assumption that initially the source is breast milk or a formula containing protein of the same quality and that between 3 and 9 months a progressive adjustment for the quality of the protein is made. The recommended intakes for infants up to 6 months are based upon observed intakes by those showing satisfactory growth. (See Table X.1.)

Vitamin A

Vitamin A is expressed in retinol equivalents (RE), which take into account the differences in vitamin A activity among the provitamins A. One RE corresponds to a biological activity in man of 1 μg of retinol, 6 μg of β-carotene or 12 μg of other carotenes as obtained from the diet. The recommended amounts are in part proportional to body weight and include arbitrary allowances for growth. (See Table X.1.)

Vitamin D

Vitamin D is expressed in terms of cholecalciferol or ergocalciferol (1 μg of either = 40 IU), which in the mammal are converted to derivatives of the same activity and potency. The recommended amounts take into account the usual amounts of exposure to sunlight in this country, and may be less if exposure is more than the usual. Excessive intakes should be avoided by allowing only those that do not greatly exceed the recommendations. (See Table X.1.)

Vitamin E

Vitamin E activity is expressed in *d*-α-tocopherol equivalents, relative to which β- and γ-tocopherol and α-tocotrienol have activities of 0.5, 0.1 and 0.3 respectively. The amount of polyunsaturated fatty acids (PUFA) to be protected is an important guide in formulating the recommended intakes. In the North American diets that have been examined, the ratio is 0.4-0.6 mg of α-tocopherol equivalent per gram of PUFA. (See Table X.1.)

Vitamin K

Compounds that are active as vitamin K are derivatives of 2-methyl-1,4-naphthoquinone and they are obtained from both the diet and intestinal bacteria. There is no firm knowledge of a quantitative dietary requirement but there is scanty evidence that for the adult it may be somewhere within the range of 0.03-1.5 μg of vitamin K_1, (phylloquinone) per kilogram of body weight per day. The greatest need for it is during the time immediately after birth, when the routine prophylactic use of vitamin K_1, may be justified.

Vitamin C

The results of experiments with radioactive isotopes have indicated that ascorbate is metabolically turned over in the body of the adult male at a rate of the order of 40 mg/day. This is taken as the basal figure for the estimation of a recommended intake. Adjustment for incomplete absorption and addition to cover individual variability produce a figure of 60 mg/day, which is the recommended intake for the young adult male. Extension to the female and to other age groups is based on the assumption that the requirement is related to body size in a manner analogous to the relationship between body size and the basal metabolic rate (BMR). On that basis the recommended amount for the young adult female is 45 mg/day. No adjustment for differences in weight or for increasing age is made. Infants fed at the breast receive 23-38 mg of ascorbic acid per day, but 7 mg/day protects against scurvy. A recommended amount of 20 mg/day is considered adequate for growth and the acquisition of stores. This is applied up to the age of 4 years, after which adjustment to the BMR is made. (See Table X.1.)

Thiamin

The requirement for thiamin is related to energy in a ratio of about 0.3 mg/1000 kcal (0.36 mg/5000 kJ) to prevent signs of depletion. Adjustment to allow for individual variability produces a figure of 0.4 mg/1000 kcal (0.48 mg/5000 kJ) as a recommended intake, but as a precaution, a minimum of 0.8 mg/day is recommended for people 19 years of age and older.

Riboflavin

Riboflavin is required in amounts related to the expenditure of energy within the range 0.25-0.35 mg/1000 kcal (0.30-0.42 mg/5000 kJ), and its urinary excretion increases sharply when the dietary intake increases beyond 0.5 mg/1000 kcal (0.6 mg/5000 kJ). This is taken as the recommended intake, but as a precaution, a minimum of 1 mg/day is recommended for people 19 years of age and older.

Niacin

Niacin is expressed as niacin equivalents (NE), 1 NE being 1 mg of niacin or 60 mg of tryptophan (about 3% of ingested tryptophan is oxidized to niacin). Requirements are expressed in relation to energy. An amount of 4.4 NE/1000 kcal (5.3 NE/5000 kJ) has been shown to prevent signs of deficiency but approximately 5.5 NE/1000 kcal (6.6 NE/5000 kJ) are required to produce an increase in the urinary excretion of niacin metabolites. To account for differences in the contribution of tryptophan and the availability of niacin from foods as well as individual variation in a population, an intake of 7.2 NE/1000 kcal (8.6 NE/5000 kJ) is recommended, but as a precaution, intakes below 14.4 NE/day are not recommended for people 19 years of age and older.

Vitamin B_6

Vitamin B_6 is involved in the metabolism of amino acids and the intake should be proportional to that of protein. All of the information on this relationship indicates that the ratio is about 15 μg of the vitamin, expressed as pyridoxine, per gram of protein. This is the recommended amount for all population groups and under all conditions except that an additional 0.3 mg/day is recommended for lactation.

Folacin

About 100 μg of pteroylglutamic acid per day prevents the development of deficiency of folacin. To derive a recommended intake, this basic figure is adjusted to account for incomplete absorption and low efficiency of utilization of polyglutamates from a mixed diet. The resulting figure of 236 is more than the average intakes of 205 and 149 μg/day, respectively, by men and women in Canada, but those amounts are apparently sufficient to prevent deficiency and maintain adequate stores. From these considerations, the recommended dietary intake of total folate is 3 μg/kg of body weight per day for adults. Larger amounts per unit of body weight are recommended for children up to 13 years of age. (See Table X.1.)

Vitamin B_{12}

Doses of 0.5-1.0 μg of vitamin B_{12} per day produce a satisfactory haematological response in patients with pernicious anaemia and meet their requirements for it. The available information indicates that 1 μg/day prevents deficiency but probably is not enough to maintain sufficient body stores. To allow for this and for variation in absorption and other factors, an intake of 2 μg/day is recommended for adults. Infants that develop deficiency of vitamin B_{12} respond to intakes of 0.1 μg/day. To allow for individual variability, growth and the maintenance of body stores, an intake of 0.3 μg/day is recommended for infancy, and

beyond that, progressive increases up to the adult level. (See Table X.1.)

Biotin

Biotin is obtained from food and also from intestinal bacteria that synthesize it in unknown amounts. Great variations in apparently adequate dietary intakes have been reported, 1.5 μg/kg of body weight per day being within the upper range. There is no indication that that amount does not cover the requirements of all population groups. Valid estimates of requirements and consequently of recommended intakes cannot be made.

Pantothenic Acid

Pantothenic acid is excreted in the urine by people whose dietary intakes vary from 3 mg/day upward, and intakes of 1 mg/day for 1.5 years have protected against deficiency. An intake of 7 mg/day, which is approximately 2.3 mg/1000 kcal (2.8 mg/5000 kJ) is within the lower range of customary intakes, and studies on adults have indicated that that amount covers the requirement. An infant that receives the same amount in relation to the energy intake would obtain about 1.6 mg/day; and an intake of 2 mg/day, which takes variability into account, is regarded as appropriate.

Calcium

Calcium is absorbed and retained by adults in increasing amounts with increasing intakes up to 10 mg/kg of body weight per day, after which both processes are less efficient. That level of intake, with an upward adjustment to account for individual variability,.becomes about 900 and 700 mg/day, which are the recommended amounts for adult men and women respectively. Breast milk provides an average of about 250 mg of calcium per day, about two-thirds of which is retained by an infant. In consideration of the variability in the secretion and intake of breast milk and of other dietary and physiological factors that become involved during that period, the recommended intake for the first 6 months is 40% above that. For age groups up to and beyond young adulthood, differences in the recommended intakes are based upon differences in the mass and condition of the skeleton. (See Table X.1.)

Phosphorus

Phosphorus in amounts equal to those of calcium are considered adequate for the requirements of growth, maintenance, pregnancy and lactation.

Magnesium

Magnesium is absorbed less efficiently with increasing intakes. An intake of 3.4 mg/kg of body weight per day has maintained balance in all adult subjects that have been studied, and this is the recommended intake for adults. Recommended amounts range from 7 mg/kg per day for infants, which is about 117% of that obtained from breast milk, down to 4.5 mg/kg per day for older children and adolescents. Quantitative requirements for skeletal growth have not been adequately defined. (See Table X.1.)

Iron

Iron is required in an amount to cover losses from the body and accretion, including sufficient to establish and maintain a store. In the young adult man and woman, these amounts are of the order of 1.25 and 2.75 mg/day, respectively, when variability among the population and menstrual loss by the woman are taken into account. The type of diet consumed by adult Canadians is such that the upper limit of absorption of its iron content is estimated to be 15%. Application of this factor produces the figures for recommended dietary intake. Recommended amounts for children and adolescents are calculated by the same procedure. For the infant it is assumed that breast milk is the source of iron up to 2 months of age and thereafter a mixed diet from which 15% of the iron is absorbed. (See Tables VIII.1. and X.1.)

Iodine

Iodine must be supplied to the thyroid in an amount of about 60 μg/day to ensure an adequate production of thyroid hormones. Positive balance is maintained on intakes of 44-162 μg/day, and 160 μg/day is the recommended intake for adults and adolescents. Breast milk contains 4-9 μg/100 kcal (1-2 μg/100 kJ) and infant formulae sold in Canada contain 5 μg/100 kcal (1.2 μg/100 kJ). The latter amount is the recommended intake for infants, which is similar to that recommended for adults when their requirement is related to energy. The amounts recommended for children are also based on their energy requirements. (See Table X.1.)

Zinc

Zinc is absorbed from a diet such as that of Canadians to the extent of up to 30%. The recommended intakes for children and adults are based on a daily obligatory loss of 90 $\mu g/kg^{0.75}$, a growth requirement of 0.3 mg/day, a factor of 1.3 for individual variability and 30% absorption. For infants, the recommended amount for the first 2 months is the amount that would be supplied by breast milk, from which the bioavailability is higher than that from cow's milk. After that age,

efficiency of absorption from the food is taken as being the same as that for other age groups. (See Table X.1.)

Copper

Copper in amounts of 1-2 mg/day may cover the nutritional requirements of children and adults, according to balance and metabolic studies that have been made, and there is support for the statement that 2 mg/day is greater than their requirements. This is close to the amount provided by the average Canadian diet. It has been estimated that infants require 50-100 μg/kg of body weight per day and that about 80 μg/kg per day is probably adequate.

Fluoride

Fluoride is obtained in amounts of 2-5 mg/day by adult Canadians who use a fluoridated water supply. Intakes of fluoride at those levels do not affect the fluoride content of breast milk, which contains an average amount of about 0.05 mg/kg (parts per million (ppm)). A suckling infant would therefore receive an amount of the order of 0.04 mg/day. It is generally accepted that near maximum dental benefits are obtained at concentrations of 0.7-1.0 ppm in drinking water in temperate climates, with no adverse changes in teeth and bones.

Manganese

Manganese is obtained from a typical Canadian diet in amounts of 2.0-4.1 mg/day. Balance studies have shown that intakes of 2.5 mg/day and higher produce positive metabolic balance. Breastfed infants receive 0.5-0.9 μg/kg of body weight per day. Formulae for infant feeding in Canada are required to contain at least 5 μg/100 kcal (1.2 μg/100 kJ).

Selenium

Selenium is obtained from a typical Canadian diet in an average amount of about 200 μg/day but there is wide variation. There is support for the statement that as little as 25 and 5 μg/day, respectively, cover the possible requirements of adults and infants; and on the other hand, that as much as 70 μg/day is required to maintain plasma levels and body stores in adults.

Chromium

Chromium is present in typical western diets in amounts to supply an adult with 50-100 μg/day. Average intakes by infants in Canada are 30-60 μg/day. No estimates of requirements for any age group can be made.

Other Trace Elements

Molybdenum, tin, vanadium, silicon and nickel have been shown

to be required nutrients for experimental animals. Typical western diets contain amounts of the first four, in the order named, to supply an adult with 120-240 μg, 100-1400 μg, 10-30 μg and 1.0-1.4 g per day. Symptoms that may be attributable to a deficiency of any of these have not been observed in humans under ordinary dietary conditions.

Water

The average amount of water ingested by adults in a temperate environment, including water of oxidation, is about 2.5 L/day, but there is wide variation. Ordinarily the intake balances the loss. The requirement of adults has been generally estimated to be about 1 L/1000 kcal (1.2 L/5000 kJ) of food energy. Since losses from infants are higher than those from adults, the requirements of infants are estimated to be 1.5 times or 1.5 L/1000 kcal except when they are breastfed.

Sodium, Potassium and Chloride

The total minimal losses of electrolytes by adults are approximately 6 mg of sodium, 20 mg of potassium and 9 mg of chloride per kilogram of body weight per day. Additions for a margin of safety and individual variability produce figures of 9, 30 and 14 mg/kg per day, respectively, which are the recommended intakes. Requirements for growth from infancy to maturity are estimated to be less than 23, 39 and 35 mg of these three, in the order named above, per day. After appropriate adjustments, 35, 70 and 50 mg/kg of body weight per day, respectively, are taken as sufficient to cover requirements for growth and maintenance up to adulthood.

Table X.1 Summary Examples of Recommended Nutrient Intakes for Canadians[a,b]

				Fat-Soluble Vitamins			Water-Soluble Vitamins			Minerals				
Age	Sex	Weight (kg)	Protein (g/day)[c]	Vitamin A (RE/day)[d]	Vitamin D (μg/day)[e]	Vitamin E (mg/day)[f]	Vitamin C (mg/day)	Folacin (μg/day)[c,g]	Vitamin B_{12} (μg/day)	Calcium (mg/day)	Magnesium (mg/day)[c]	Iron (mg/day)	Iodine (μg/day)	Zinc (mg/day)
Months														
0-2	Both	4.5	11[h]	400	10	3	20	50	0.3	350	30	0.4[i]	25	2[j]
3-5	Both	7.0	14[h]	400	10	3	20	50	0.3	350	40	5	35	3
6-8	Both	8.5	17[h]	400	10	3	20	50	0.3	400	50	7	40	3
9-11	Both	9.5	18	400	10	3	20	55	0.3	400	50	7	45	3
Years														
1	Both	11	19	400	10	3	20	65	0.3	500	55	6	55	4
2-3	Both	14	22	400	5	4	20	80	0.4	500	70	6	65	4
4-6	Both	18	26	500	5	5	25	90	0.5	600	90	6	85	5
7-9	M	25	30	700	2.5	7	35	125	0.8	700	110	7	110	6
	F	25	30	700	2.5	6	30	125	0.8	700	110	7	95	6
10-12	M	34	38	800	2.5	8	40	170	1.0	900	150	10	125	7
	F	36	40	800	2.5	7	40	180	1.0	1000	160	10	110	7
13-15	M	50	50	900	2.5	9	50	150	1.5	1100	210	12	160	9
	F	48	42	800	2.5	7	45	145	1.5	800	200	13	160	8
16-18	M	62	55	1000	2.5	10	55	185	1.9	900	250	10	160	9
	F	53	43	800	2.5	7	45	160	1.9	700	215	14	160	8
19-24	M	71	58	1000	2.5	10	60	210	2.0	800	240	8	160	9
	F	58	43	800	2.5	7	45	175	2.0	700	200	14	160	8
25-49	M	74	61	1000	2.5	9	60	220	2.0	800	250	8	160	9
	F	59	44	800	2.5	6	45	175	2.0	700	200	14[k]	160	8

Table X.1 Summary Examples of Recommended Nutrient Intakes for Canadians[a,b]

Age	Sex	Weight (kg)	Protein (g/day)[c]	Fat-Soluble Vitamins			Water-Soluble Vitamins			Minerals				
				Vitamin A (RE/day)[d]	Vitamin D (μg/day)[e]	Vitamin E (mg/day)[f]	Vitamin C (mg/day)	Folacin (μg/day)[g]	Vitamin B_{12} (μg/day)	Calcium (mg/day)	Magnesium (mg/day)[f]	Iron (mg/day)	Iodine (μg/day)	Zinc (mg/day)
50-74	M	73	60	1000	2.5	7	60	220	2.0	800	250	8	160	9
	F	63	47	800	2.5	6	45	190	2.0	800	210	7	160	8
75+	M	69	57	1000	2.5	6	60	205	2.0	800	230	8	160	9
	F	64	47	800	2.5	5	45	190	2.0	800	220	7	160	8
Pregnancy (additional)														
1st Trimester			15	100	2.5	2	0	295	1.0	500	15	6	25	0
2nd Trimester			20	100	2.5	2	20	295	1.0	500	20	6	25	1
3rd Trimester			25	100	2.5	2	20	295	1.0	500	25	6	25	2
Lactation (additional)			20	400	2.5	3	30	120	0.5	500	80	0	50	6

Footnotes to Table X.1

[a] Recommended intakes of energy and of certain nutrients are not listed in this table because of the nature of the variables upon which they are based. The figures for energy are estimates of average requirements for expected patterns of activity (see Table II.1). For nutrients not shown, the following amounts are recommended: thiamin, 0.4 mg/1000 kcal (0.48 mg/5000 kJ); riboflavin, 0.5 mg/1000 kcal (0.6 mg/5000 kJ); niacin, 7.2 NE/1000 kcal (8.6 NE/5000 kJ); vitamin B_6, 15 μg, as pyridoxine, per gram of protein; phos phorus, same as calcium.

[b] Recommended intakes during periods of growth are taken as appropriate for individuals representative of the mid-point in each age group. All recommended intakes are designed to cover individual variations in essentially all of a healthy population subsisting upon a variety of common foods available in Canada.

[c] The primary units are expressed per kilogram of body weight. The figures shown here are only examples. See text.

[d] One retinol equivalent (RE) corresponds to the biological activity of 1 μg of retinol, 6 μg of β-carotene or 12 μg of other carotenes.

[e] Expressed as cholecalciferol or ergocalciferol.

[f] Expressed as *d*-α-tocopherol equivalents, relative to which β- and γ-tocopherol and α-tocotrienol have activities of 0.5, 0.1 and 0.3 respectively.
[g] Expressed as total folate.
[h] Assumption that the protein is from breast milk or is of the same biological value as that of breast milk and that between 3 and 9 months adjustment for the quality of the protein is made.
[i] It is assumed that breast milk is the source of iron up to 2 months of age.
[j] Based on the assumption that breast milk is the source of zinc for the first 2 months.
[k] After the menopause the recommended intake is 7 mg/day.